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TITLE: Field Testing of Meningococcal Group B Vaccine and Oral  
Cholera Vaccine

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DR. JORGE TORO

PI - Signature

Oct 96

Date

## TABLE OF CONTENTS

COVER . . . . .	i
REPORT DOCUMENTATION PAGE . . . . .	ii
FOREWORD . . . . .	iii
TABLE OF CONTENTS . . . . .	iv
INTRODUCTION . . . . .	1
LABORATORY ACTIVITIES . . . . .	1
PARALLEL LABORATORY ACTIVITIES . . . . .	4
ADMINISTRATIVE ASPECTS . . . . .	8
FINAL CONCLUSIONS . . . . .	10
APPENDICES . . . . .	12

[DTIC QUALITY INSPECTED 3]

FINAL REPORT OF PROJECT ON RESEARCH  
INTO THE MENINGOCOCCAL DISEASE  
IQUIQUE 1991 - 1995

## INTRODUCTION

From 1987 to 1990, in the city of Iquique, Chile, efficacy tests were carried out on a group B anti-meningococcal vaccine, which had been prepared by a group headed by Dr. Wendell Zollinger in the W.R.A.I.R in Washington D.C.

This study, as was informed in previous reports, showed a 51% efficacy for all age groups under study (1 to 21 years of age). In children of 1 to 4 years of age the vaccine provided no protection with an efficacy of -23% after 30 months of follow-up; but in the volunteers aged 5 to 21 the efficacy was found to be 70% during that same period.

These results, which are not by any means satisfactory, were promising and allowed investigation to be continued in the search for a more effective vaccine. For this reason, it was decided to keep the research laboratory in Iquique going for the period 1991 through 1994.

## LABORATORY ACTIVITIES

### A. Active Epidemiological Surveillance of the Meningococcal Disease

After the efficacy test for the the anti-meningococcal vaccine was carried out, the research laboratory in Iquique for the meningococcal disease was kept going and its main job was maintaining an active daily epidemiological surveillance of this disease. This allowed a longer-term evaluation of the efficacy of the vaccine used in 1987 and, later, to keep reliable and updated records on the meningococcal disease rate in Iquique in the hopes of possible efficacy tests with a new vaccine.

During the period 1991 up to June 1995, the date up to which the laboratory was kept open, its activities centered principally on active epidemiological surveillance.

Within the framework of this active epidemiological surveillance the following points were taken into account:

1. Objectives

a) To determine accurately the frequency of the meningococcal disease and the antigenic characteristics of the germs causing it.

b) To determine the feasibility of carrying out efficacy tests with a new and improved group B anti-meningococcal vaccine.

c) To evaluate a new polymerase chain-reaction method for detecting the presence of meningococcus in cerebrospinal fluid.

2. Methods a) To develop a data bank which would include all cases of meningococcal infection using a record of clinical cases designed for this purpose.

3. Responsibilities

a) To identify patients with meningococcal infection.

b) To supervise the obtaining, processing and evaluation of laboratory tests indicated for each patient.

c) To do home calls for obtaining epidemiological data.

d) To coordinate all activities with the Head of the Department of Persons' Programs, whose responsibility is to notify all cases to the Ministry of Health.

For carrying out the above, daily visits were made to some of the Hospital Services (Pediatrics, General Practitioners, Intensive Care Units, Inpatients, Emergency Wards), Laboratories and private Clinics in order to record the admission of any patient suspected of having a meningeal infection.

The following was taken into account when classifying the cases for whom records were opened (Appendix 1), :

1. Confirmed case: Isolating *N. meningitidis* in cerebrospinal fluid or blood.

2. Highly suspect case: With a set of clinical signs and symptoms compatible with a meningococcal infection and the presence of *N. meningitidis* in a pharyngeal secretion culture or a Gram tinction of cerebrospinal fluid consistent with *N. meningitidis*.

3. Suspected case: With a set of clinical signs and symptoms or suspected epidemiology of meningococcal infection, but lacking any confirmed laboratory results.

The execution of these activities allowed us to build up a complete and reliable casuistry of cases of meningococcal disease in Iquique, which allowed us to prepare frequency graphs of the disease over the 1987-1995 period, and define the monthly and seasonal variations we had observed.

The analysis of these results was submitted periodically to the local Health Service (Appendix 2), rendering also our advice on aspects concerning the epidemiology of this disease, which consisted of:

1. Updating prevailing norms concerning prevention and handling of patients with meningococcal disease (Appendix 3).

2. Educational campaigns to different sectors of the community in relation to the situation of this disease at a local level.

3. Mass dissemination through the media for educating the community regarding aspects concerning the disease.

4. Delivery of information to doctors, nurses and other members of the different local health services related to different updated aspects of the meningococcal disease (Appendix 4).

5. Training courses for nurse's aides in epidemiological surveillance on a yearly basis. This was aimed at students and acting personnel.

6. Dissemination of the results obtained from the active epidimiological surveillance in the rest of the country.

## B. Parallel Laboratory Activities

By making use of the infrastructure set up and in relation to the different circumstances connected to the behavior of the epidemic of the meningococcal disease in the city of Iquique, and faced with the imminent outbreak of a new infectious-contagious disease, like cholera, several different additional activities were carried out at a local level, which are detailed as follows:

1. Project to eradicate nasopharyngeal carriers of *Neisseria meningitidis* in Cariquima. (November 1990 - December, 1991).

Faced with the disproportionate increase in the occurrence of meningococcal meningitis in 1990 among the population of Cariquima, a rural community in the Altiplano area of the province of Iquique, it was decided to act, first of all evaluating who were the nasopharyngeal carriers of meningococcus among that population and then immediately carry out mass chemoprophylaxis.

One year later a new study was done regarding nasopharyngeal carriers of meningococcus in the same persons. This made it possible to evaluate the long-term effectiveness of the treatment used for eradicating the germ mentioned above, to check the specific efficacy of Ciprofloxacin as a chemoprophylactic agent in adults over 16 years of age and to verify if a mass plan for acting in an isolated community would be effective for aborting an outbreak of the meningococcal disease.

The results revealed a high degree of effectiveness in preventing the spreading of the disease, because no new cases of meningococcal disease have been reported in that community. The number of nasopharyngeal carriers decreased sharply in the controls that were carried out one year after having done the chemoprophylaxis on nasopharyngeal meningococcus carriers. (Appendix 5)

2. Evaluation in Phase II of the immunogenicity and safety of the anti-cholera vaccine based on dead cells plus sub-unit B in a group of Chilean people aged 2 to 15 years. (January 1992 - August 1992)

As the W.R.A.I.R had a Swedish anti-cholera vaccine available, which had been subjected to research in Phases I and II in 115 adults (41 volunteers in Sweden and 74 volunteers in military contingents in the United States), with good results in relation to its immunogenicity and with minimum side-effects it

was decided to assess those same aspects in the Chilean population of children aged between 2 and 15 years.

The study included 400 children of the age range mentioned above, from the municipality of Iquique described in the municipality of Iquique, which were divided into 4 groups of 100 children each. Of these, three groups received the vaccine in two initial doses at different intervals and the fourth was the control group receiving a placebo. Twenty-six weeks after the last dose of vaccine, they were given a booster dose. The children were assigned to each group at random and it was a double-blind study.

The laboratory analysis of the samples obtained during the different stages of the study was carried out in Sweden in the Microbiology and Medical Immunology Department of the University of Goteburg, with Dr. Ann-Mari Svennerholm in charge. The compiling of all the results was done by the W.R.A.I.R, whose final conclusions have still to be sent to us.

Generally speaking, it was observed that good responses were obtained regarding the production of anti-toxin antibodies but the vibriocide activity was not so effective, with a significant decrease of both 6 months after administration of the vaccine (Appendix 6).

3. Studies of nasopharyngeal carriers of *N. meningitidis* in contacts of patients with meningococcal meningitis (May 1992 - May 1993).

Over a period of one year the prevalence rate was evaluated among healthy nasopharyngeal carriers in a population at risk such as that made up of all the contacts of patients that had shown signs of the meningococcal disease and those highly suspected of having had of it but without bacteriological confirmation.

At the same time, we wanted to evaluate and compare the efficacy of Rifampin and Ciprofloxacin in the eradication of the meningococcus in carriers, as well as comparing this carriage with similar experiences undergone in Iquique (1987) and Arica (1989) previously, but in a group from the general population.

No significant differences were observed in the carriage of the epidemic strain, but the large increase in carriers of lactamic *Neisseria*, above all in the population aged between 1 and

15 years was very noticeable. (Appendix 7)

4. Participation as speakers at the International Seminar and Workshop on "Prevention and Surveillance of Meningitis", organized by the Sub-Region for Health of Tacna and the General Administration for Epidemiology of the Peruvian Ministry of Health. (October 10 to 13, 1993. Peru)

The health authorities of the city of Tacna, faced with an outbreak of some cases of meningococcal meningitis in Peru, above all by the appearance of cases in neighboring places such as the port of Ilo, organized this seminar to which our Laboratory was invited to attend together with its professional team in order to speak of our experiences in the epidemiological surveillance of this disease and the measures that had been taken at a local as well as a national level for its prevention.

On that occasion PAHO/WHO advisers in that country took part as well. (Appendix 8)

5. Participation as speakers in the Commission on meningococcal meningitis B organized by the Chilean Society for Hygiene during the Seventh Chilean Congress on Hygiene (November 26, 1993. Santiago).

As a result of our experience with the epidemic of meningococcal meningitis B and our prior participation in Ministerial meetings, Dr. Bustamante was invited by its Sponsors to take part in this Congress (Appendix 8).

6. Participation in the SECOND WORKSHOP ON ACUTE BACTERIAL MENINGITIS (Reñaca, December 3, 1994).

Our work group was selected by the Chilean Society for Infectious Diseases, the coordinator of this event, because of the experience it has acquired on this matter, to take part in this Workshop in which clinical and epidemiological aspects concerning bacterial meningitis were analyzed and discussed. (Appendix 8)

7. Participation in the Second Chilean Congress on Epidemiology. (October 26 through 29, 1993. Santiago)

The professional team from our laboratory was invited to attend the Congress, which counted with the participation of eminent epidemiologists from the American continent (Appendix 8).

8. The study of nasopharyngeal carriers of *N. meningitidis* in the general school population aged from 1 to 19 years in the city of Iquique. (April 1995)

In 1987 a study of nasopharyngeal meningococcal carriers was carried out among a group of 1,017 children from 1 to 19 years of age, selected randomly in order to be representative of the school-age community of the whole city, chosen from out of a population in which efficacy tests of the anti-meningococcal vaccine had been done.

As a result of this experience it was decided this year to carry out a study to evaluate a population with the same characteristics as the previous one, to compare the occurrence of *N. meningitidis* carriers and the epidemic strain in both groups, bearing in mind that these experiences were at different stages of the epidemiological curve of the meningococcal disease, the first when the occurrence of this illness stood at 25.6 cases per 100,000 inhabitants and the present one standing for the year 1994 at 5.6 cases per 100,000 inhabitants.

The partial results we have show that in the present study the number of nasopharyngeal meningococcus carriers in the healthy school-age population is 7.3%; somewhat lower than the year 1987 which was 11.5%. We still do not have the number of carriers of the epidemic strain because these results are being currently prepared in the W.R.A.I.R laboratories (Appendix 8).

From these works, only the third one was presented in different health environments being presented at the Public Health Congress in Copiapó in August 1994 and at the Pediatric Congress in Concepción the same year. (appendix 9)

The other research work, although it was properly carried out and tabulated, and the results analyzed, were not worth publishing, although informative documents addressed to the local Health Authorities, to the Pan American Health Organization and the head researcher were sent out.

## ADMINISTRATIVE ASPECTS

In this second phase of the laboratory's operation, the supervision at a local level was done by Dr. Ricardo Bustamante Risco, who took over the job in March 1991. The personnel with whom Dr. Bustamante worked, and who stayed on until the project was closed was made up as follows:

Nurse: Mrs. Marcela Martínez Marco. Her task can be summarized in the following activities:

1. Assisting the doctor in charge of the project in surveillance, specially during his absence.
2. Taking blood samples for bacteriological analyses which were later carried out in the US.
3. Cooperating in administration and planning of the project.
4. Supporting in health education and information to specific community groups.
5. Tabulating data belonging to patients' records and their contacts.
6. Keeping complete and up-dated clinical and laboratory records of each patient admitted.

Medical laboratory technician: Mr. Fermín Mendez Albarracín. With the following responsibilities:

1. Obtaining proper samples for bacteriological study.
2. Preparing cultures with each of the samples obtained from patients.
3. Classifying and preserving all the cultures which were positive.
4. Recording all samples processed in the corresponding books.
5. Sending the strains of *Neisseria meningitidis* to the Institute for Public Health for confirmation and classifying serotypes.

Secretary - Auxiliary: Mrs. Blanca Chamber Lobos. With the following job assignment:

1. Assisting the nurse in laboratory and field work.
2. Assisting the supervising physician in obtaining and filing documents relating to the project.
3. Secretarial activities.
4. Post and courier jobs.
5. Cleaning and orderliness in all sections of the laboratory.

This personnel, together with the supervising physician, have done their duties constantly and regularly during the whole period the project lasted, with extra cooperation in certain circumstances whenever they were needed.

The additional activities of the laboratory mentioned in point B required the cooperation of nurses, nurse's aides and medical laboratory technicians who were paid for the time they did their respective jobs.

Physicians and medical laboratory technicians from the W.R.A.I.R. ESC R 07H took part in the study of the immunogenicity and safety of the anti-cholera vaccine,.

## FINAL CONCLUSIONS

The main objective of maintaining active epidemiological surveillance of the meningococcal disease in the city of Iquique was to obtain the most reliable data possible in relation to annual occurrence, before carrying out an evaluation of safety and immunogenicity of a new anti-meningococcal vaccine.

This vaccine was being studied at the W.R.A.I.R. and was put under study in phases I and II in a group of adult volunteers. The results obtained from these studies did not show, finally, that the response regarding the production of antibodies or the bacteriological activity were any better than those obtained with the vaccine previously used in Chile in 1987. For this reason, the possibility of carrying out phases I and II with this vaccine in our country was rejected.

In spite of the impossibility of reaching this final objective, the fact that a laboratory was kept going with active surveillance (a unique experience with this pathology together with Antofagasta in our country) allowed us to find clear and timely evidence regarding several epidemiological aspects of the meningococcal disease so as to tackle them in its early stage and with greater efficiency.

The meningococcal disease in the city of Iquique had extremely high occurrence rates; something unheard of in our country, reaching its highest point of 29.2/100,000 with a gradual decline thereafter. However, over the past four years we experienced a sharp decrease in occurrences that could correspond to the natural evolution of the epidemiological curve, but we believe that the prevention actions carried out by the local Health Service, indicated and under the advise of our laboratory also had a lot to do with it.

Our work also allowed to build up a local epidemiological profile of all the infectious meningeal pathologies, whose information has been of great usefulness in the overall aspects of their handling in specific areas of health as well as in the clinical field.

In this way, we believe that it is essential to maintain an Active Epidemiological Research Laboratory in our city, not only directed towards the meningococcal disease but also to other infectious and contagious diseases at a local community level as well as within the hospitals. This will allow us to continue

working on a reliable and timely epidemiological profile of the health environment in our city which will clearly point the way for our policies for action at whatever different levels they are required.

A P P E N D I C E S

Meningococcal Vaccine Efficacy by Age Group in Iquique  
Chile 1987 - 1990  
Culture Confirmed Cases

## Record Sheet of Clinical Cases

Case N° \_\_\_\_\_

Date Admitted \_\_\_\_\_ Date Discharged \_\_\_\_\_

Definition of Case \_\_\_\_\_ (Definite/Suspect/Neither)

A study patient ? \_\_\_\_\_ (Yes / No)

Study N° \_\_\_\_\_

Date of 1<sup>st</sup> dose \_\_\_\_\_ Date of 2<sup>nd</sup> dose \_\_\_\_\_

Diagnosis on discharge \_\_\_\_\_

Clinical Record N° \_\_\_\_\_

NAME \_\_\_\_\_

Father's Surname Mother's Surname Given Names

Address \_\_\_\_\_ Sector \_\_\_\_\_

Age \_\_\_\_\_ Date of Birth \_\_\_\_\_ Sex \_\_\_\_\_ (M/F)

Name of establishment \_\_\_\_\_ Code \_\_\_\_\_

Course \_\_\_\_\_ Letter \_\_\_\_\_ Time \_\_\_\_\_ (M, A or N)

### Clinical information

Consulted at: E.S. \_\_\_\_\_ Other \_\_\_\_\_ (specify):

Date the symptoms began: \_\_\_\_\_

Date of consultation: \_\_\_\_\_

Symptoms - type and severity:

Fever \_\_\_\_\_ (Yes/No) Maximum temperature \_\_\_\_\_

Gastrointestinal

Anorexia (none - marked: 0 to 3) \_\_\_\_\_

Nausea \_\_\_\_\_ (yes/No)

Abdominal pains \_\_\_\_\_ (yes/No)

Vomiting (none - much : 0 - 2) \_\_\_\_\_

Diarrhea \_\_\_\_\_ (yes/No)

Head ache (none - much: 0 to 2) \_\_\_\_\_

Activity (hiccups, normal, hyper) \_\_\_\_\_

Consciousness (conscious, confused or in coma) \_\_\_\_\_

Convulsions (yes/No) \_\_\_\_\_ Hemorrhagic eruptions

Previous treatment with antibiotics ? \_\_\_\_\_ (Yes/No) \_\_\_\_\_

Others:

### Results of the physical examination

Height \_\_\_\_\_ Weight \_\_\_\_\_ Temp. ° \_\_\_\_\_ Pulse Rate \_\_\_\_\_ Blood Pressure \_\_\_\_\_

\_\_\_\_\_ cm \_\_\_\_\_ Kg \_\_\_\_\_ C° \_\_\_\_\_ / \_\_\_\_\_

Any meningeal signs ? (Yes/No) \_\_\_\_\_

Any hemorrhagic eruptions ? (none or all over the body: 0 to 4) \_\_\_\_\_

Type (petechial, purpura, combined) \_\_\_\_\_

Diagnosis on admission: \_\_\_\_\_

## Laboratory examinations

CSF:

Bacteriological exam:

Date: \_\_\_\_\_  
Day Mth Year

Results of Gram tinction

(for example: ngd = negative  
gm diplococcus, pgc = positive  
gram coccus)

Culture (organism) \_\_\_\_\_ Group \_\_\_\_\_

Sample N° (Access N° in Iquique) \_\_\_\_\_

Sample N° (Access N° in Santiago) \_\_\_\_\_

Sensitivity to antibiotics.

Chemi \_\_\_\_\_ Penicillin \_\_\_\_\_ Rifampin \_\_\_\_\_ Eritromicin \_\_\_\_\_

## Cytochemical Exam:

Sample N° (Access N° in Iquique) \_\_\_\_\_

Aspect (transparent, cloudy, opalescent) \_\_\_\_\_

Color \_\_\_\_\_ Sediment \_\_\_\_\_

Protein (gm %) \_\_\_\_ Glucose (gm %) \_\_\_\_

Leukocytes (/mm<sup>3</sup>) \_\_\_\_\_

PMN (%) \_\_\_\_\_

MN(%) \_\_\_\_\_

Erythrocytes (/mm<sup>3</sup>) \_\_\_\_\_

## **Blood test:**

Cultures

Date Isolated Sample N° (Access N° in  
Iquique)

Hemoculture 1

Hemoculture 2

Hemoculture 3

Group

Sample N° (Access N° in Santiago) \_\_\_\_\_

Sensitivity to antibiotics.

Chemi \_\_\_\_\_ Penicillin \_\_\_\_\_ Rifampin \_\_\_\_\_ Eritromicin \_\_\_\_\_

Hemogram: Date \_\_\_\_\_ Hematocrit value (%) \_\_\_\_\_ ESR (mm/hr) \_\_\_\_\_

Leucocytes (x10<sup>3</sup> /mm<sup>3</sup>) \_\_\_\_\_

Monocytes (%) \_\_\_\_\_ L \_\_\_\_\_ Seg \_\_\_\_\_ B \_\_\_\_\_ Juv \_\_\_\_\_

Smear Blood Platelet \_\_\_\_\_ (Normal, Increased, Decreased)

Smear of Pharynx sample

Date \_\_\_\_\_ Culture (organism) Sample N° (Access N° in  
Iquique) \_\_\_\_\_ Group \_\_\_\_\_

Sample N° (Access N° in Santiago) \_\_\_\_\_

Sensitivity to antibiotics.

Chemi \_\_\_\_\_ Penicillin \_\_\_\_\_ Rifampin \_\_\_\_\_ Eritromicin \_\_\_\_\_

Evolution in Hospital

Normal evolution (48-72 hrs: without fever, cooperative, active, hungry) \_\_\_\_ (Yes/No)

Treatment (Penicillin, Ampi, Genta, Chemi, etc.)

Drug N° 1 \_\_\_\_\_

Drug N° 2 \_\_\_\_\_

Dose and sufficient time ? \_\_\_\_ (Yes/No)

Drug N° 3 \_\_\_\_\_

4 \_\_\_\_\_

5 \_\_\_\_\_

Complications:

1 \_\_\_\_\_

2 \_\_\_\_\_

3 \_\_\_\_\_

Condition on

discharge: 1 = alive and apparently without consequences

2 = alive with consequences

3 = deceased \_\_\_\_\_

Description: \_\_\_\_\_

Follow-up:

Date of medical control \_\_\_\_\_

Results of physical examination:

Diagnostic of follow-up control :

Summary of Samples

Serum                      date obtained      Date Preserved      Sample N°

Acute

Convalescent

Bacteriology

CSF (acute)

Gram Tinction

Culture

Blood

Nasopharynx

Other

REPORT OF ACTIVITIES  
JULY - OCTOBER 1991

EPIDEMIOLOGICAL SURVEILLANCE

Epidemiological surveillance continues checking in detail each one of the cases that is admitted to this Hospital and taking serum samples from acute and convalescent patients with confirmed or suspected diagnosis of meningitis.

From January to date we have :

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	TOTAL
Conf.MM	1	2	1	0	1	2	1	4	2	1	15
Asoc.MM				1			1	1			3
Susp.MM	3	3	1		1						8
Others			2	2	2			1	1	7	15
Total	4	5	4	3	4	2	2	6	3	8	41

Meningococcal meningitis (distribution according to ages)

-1 year old = 1  
 2 to 5 years old = 5  
 6 to 14 years old = 4  
 15 to 20 Years old = 1  
 21 years and over = 4

Out of all the cases of Meningitis accumulating to date, we have 4 deaths corresponding to the following cases :

Purulent Meningitis (SOS) = 1 57 years of age  
 Meningitis Haemophilus = 1 7 months old  
 Meningococcemia = 1 2 years old  
 Meningitis Staphylococcia = 1 60 years of age  
 Meningitis Streptococcus B Hemolytic 1 RN

During the month of October there was an accumulation of cases of Meningitis in the Neonatology Service, where one of the cases of B Hemolytic Streptococcus was detected. The rest of the patients

admitted had an altered CSF, but a negative Gram and negative CSF culture and hemoculture.

Those patients with a confirmed or suspected diagnosis of meningococcal meningitis or SOS are visited in their homes in order to record their social, economic and clinical background and personal history and if their contacts have been treated or not. Some times the visits have to be repeated in order to take a serum sample of the convalescent patient.

Home Visits	20
Taking samples of serum of convalescent patients	14

#### OTHERS

On the 8 July 1991, a report was sent to Santiago on the request of Dr. Toro regarding the Laboratory's monthly average expenses (a photocopy is attached of request, Appendix 1)

A list was made of the needs for beginning epidemiological surveillance in Antofagasta and contact was maintained with this Service by facsimile (the list sent is attached, Appendices 2 and 3).

The Health Service of Antofagasta sent a nurse from the DPP to see our Laboratory running so as to adapt it to the needs of that city.

Between the 7 and 9 August, professionals from the laboratory attended a workshop on Epidemiological Surveillance in Hospital Infections carried out in Iquique and organized by the Ministry of Health.

With the object of updating the new Physicians and Paramedics of the Hospital on epidemiological surveillance of Meningitis and to bring it up to date for the older ones, a circular was sent to the different hospital Services. Circular attached (appendix 4 and 5).

From the 26 to 30 August, professionals from the Laboratory attended a workshop on Basic Epidemiology for Primary Health Care Teams organized by the Ministry of Health in Iquique. A Program on Primary Health Care together with the *Cooperazione Italiana*.

A training program in Epidemiology for the students in the nurse's aides course was planned for the month of November.

The Institute for Public Health was requested to send Hemoglobin and Agar CTA in order to determine the Neisseria species. This was sent, but was of no use because it had expired.

The Hospital has it on its list of pharmacological purchases but it has still not arrived.

#### PERSONNEL

Up to this moment, the following personnel continue working in the Laboratory:

1 physician by the hour

1 full-time nurse

1 nurse's aide/courier for 1/2 day

2 medical laboratory technicians by the hour.

#### FINANCIAL ASPECTS

At this point in time we are working without any resources whatsoever.

The Health Service is the authority that has shouldered all the expenses for maintaining the Laboratory since June, 1991.

Expenditure for the months of June through September 1991 is attached.

This situation worries us, because should there be the possibility of an outbreak of meningococcal meningitis in Iquique we feel that we are not prepared to act immediately without the necessary funds.

The doctor as well as the nurse pay for their own gasoline for:

Traveling to and from work

Home Visits

Laboratory Work outside

Meetings with the health service, local government, schools and the community in general.

Training

The nurse's aide must pay from her own pocket traveling expenses to and from work and she has no other source of income.

Even so, this Laboratory has kept going unrelentlessly with all its personnel intact for the four months that it has been lacking funds, and we hope this will be taken into account when we are in better financial shape.

At this moment funds have been remitted from WRAIR to the PAHO in Washington which we hope to use shortly and once all paperwork has been overcome.

yours faithfully,  
Marcela Martínez H  
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\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
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Laboratory for Research  
into Meningitis - Cholera

REPORT ON ACTIVITIES  
NOVEMBER 1991 - MARCH 1992

A. EPIDEMIOLOGICAL SURVEILLANCE OF MENINGOCOCCAL MENINGITIS

During this period, active surveillance of meningococcal meningitis was continued, therefore we now have updated information on the situation with regard to this disease in Iquique.

During the year 1991, 45 cases of bacterial meningitis were recorded, see Table I, the meningococcal etiology being still predominant.

TABLE I.

<u>Etiology</u>	<u>N° of cases</u>
Neisseria meningitidis	19
Hemophilus influenzae	02
Streptococcus pneumoniae	04
Streptococcus group B	03
TBC	01
Golden staphylococcus	01
Unknown origin of germs	15

The distribution by ages of meningococcal meningitis was as follows:

≤ 1 year old	=	2
≥ 2 years and ≤ 5 years old	=	6
≥ 6 years and ≤ 14 years old	=	7
≥ 15 years and ≤ 20 years old	=	2
> 20 years old	=	5
TOTAL	=	22

Exceeding the total amount indicated in Table 1 by three cases, because those classified as highly suspect were included here, which correspond to patients whose CSF was altered and who presented clinical signs and symptoms consistent with meningococcal meningitis but who had negative cultures.

The total number of deaths due to meningococcal meningitis was 7 cases, 3 of them corresponding to meningococcal etiology which showed a set of signs and symptoms consistent with meningococcemia. This gives us a specific mortality rate for this disease of 13.6% for the year 1991.

So far this year, 1992, there have been a total of 13 cases of bacterial Meningitis and its etiological distribution is shown in the following table:

<u>ETIOLOGY</u>	<u>Cases</u>
N. meningitidis	8
Haemophilus influenzae	2
Streptococcus pneumoniae	1
Aseptic (viral?)	1
<u>Unidentifiable</u>	<u>1</u>
Total to this date	13

This last unidentified case was highly suspected to be of meningococcal etiology, because the signs and symptoms and the CSF cytochemical test were both consistent with it; but N. meningitidis was isolated only in the pharyngeal smear, all other cultures being negative.

The distribution by age of the meningococcal meningitis is:

<u>AGE RANGE</u>	<u>Cases</u>
≤ 1 year old	2
1 to ≤ 10 years of age	5
11 to ≤ 20 years of age	1
Nº of children	<u>8</u>

During the same period in 1991 6 cases had been confirmed as group B meningococcus meningitis from the same epidemic strain that had been predominant over the past 6 years in Iquique.

It is worth mentioning that since last year Dr. Wendell Zollinger, in charge of this investigation at the WRAIR, has been carrying out a new PCR method for detecting meningococcus in the samples taken from patients. This has allowed the presence of the meningococcal infection to be confirmed or rejected in those cases which were initially labeled as being suspect or highly suspect or even not meningococcal at all. This has slightly modified the incidence rates of this etiology over the past three years.

(Appendices 1A and 1B)

Active epidemiological surveillance of meningococcal meningitis will remain unaltered until December 1992, but this must be defined on October of this year depending on the incidence of this disease in Iquique and the possibility of doing an efficacy test with a new and improved group B anti-meningococcal vaccine, if this work continues. (Appendices 2A and 2B)

With regard to the active surveillance plan of the meningococcal disease, modifications were done related to the objective pursued, because there is still no group B meningococcal vaccine to be evaluated. The present objectives are:

1. To determine precisely the incidence of the meningococcal disease and the antigenic characteristics of the germs which cause it.
2. To determine the feasibility of carrying out an efficacy test of a new an optimized group B vaccine.
3. To evaluate a new PCR method for detecting meningococcus in CSF.

#### B. A STUDY OF PHARYNGEAL CARRIERS OF MENINGOCOCCUS IN CARIQUIMA

In December 1991 (from 11 through 13) in the town of Colchane and its surroundings, an Altiplano community almost on the border with Bolivia, a control study of pharyngeal carriers of meningococcus was carried out among its population. This community had received in December 1990, prior to the initial evaluation of pharyngeal carriers of meningococcus, chemoprophylaxis with Ciprofloxacin, which was administered to adults over 16 years of age and Rifampin which was given to persons under that age, in order to eradicate the group B meningococcus in the pharynx. Although the epidemic strain of B:15:1.3 was only found in eight of the community members, the entire community got treatment, covering a total of 351 persons including the carriers of the epidemic strain.

After a year had passed since this eradication, a control study was done of the pharyngeal carriers of meningococcus in this same community. This time, 306 persons were evaluated of those treated (87.2%) and 7 out of the 8 who had previously carried the epidemic strain (87.5%); the epidemic strain was found only in one

female youngster who in the previous evaluation had shown no signs of it. She will undergo a new test to detect pharyngeal meningococcus and will be given chemoprophylaxis. Since December 1990, there have been no new cases of meningococcal meningitis in this sector of the Andes.

The obtaining of results from pharyngeal meningococcal carriers by the Public Health Authorities coincided with the period in which our laboratory was dedicating almost all its time to studying the vaccine against cholera (see further on), and for this reason an exhaustive analysis has still not been made of the results. (Appendices 3 and 4)

#### C EVALUATION OF IMMUNOGENICITY AND SAFETY IN PHASE II OF THE VACCINE AGAINST CHOLERA BASED ON DEAD CELLS PLUS SUB-UNIT B (WC/rBS).

In answer to a proposal from a group of researchers from WRAIR, headed by Dr. Robert A. Kuschner, it was decided to make an evaluation of phase II of a vaccine against cholera manufactured in Sweden on a group of children between 2 and 15 years of age in the city of Iquique. This vaccine is similar to the one manufactured by Merieux and which was applied in 1985 in Bangladesh, but the method used for obtaining sub-unit B in it was very costly and slow. The present vaccine uses a recombinant technology of DNA for the production of this sub-unit.

As the date scheduled for beginning this study was 20 January (summer holiday period in our country), a series of activities were scheduled as of mid-December 1991 in order to get together the necessary number of children for this purpose. Thanks to the press and with the help of Dr. Jorge Toro and Dr. Patricia Gassibe (Ministry of Health), this vaccination was given a lot of initial publicity, after a meeting with the medical community in our city (Appendices 4A and 4B). Then with the support of Drs. Ramses Aguirre and Eduardo Olguin, the local health authorities, information was disseminated over local and national television.

Through the National Association of Kindergartens, meetings were organized with the parents and tutors of children from different Kindergartens in the city, in order to explain to them the aims of our work and obtain their cooperation. It should be pointed out very clearly that all the children included in this study were volunteers; the parents having signed a letter of

consent before taking part in the study.

These meetings were also designed to include the parents of children in different places where it was possible to gather a large number of children who could be relatively easy to locate. This was published by all the local press and on custom-designed posters. Meetings were organized in the three outpatient clinics belonging to the Municipal Corporation for Social Development, in Women's and Men's Homes belonging to the Police Force, in the Hogar del Niño (Children's Home), Day Care Centers, Youth Care Centers and with community committees in the townships of Primeras Piedras and Alto Hospicio. These two latter communities are high risk areas for cholera, due to the neglected conditions in which the inhabitants live, made even worse by the lack of proper sanitation and hygiene in this sector.

The first stage of the vaccination was carried out between 20 January and 27 March of this year, and included the incorporation of 485 children between the ages of 2 and 15 (232 of or younger than five years and 253 older than five). These were then divided randomly into four groups, one of them being the control group who was administered a dose of a placebo and the rest received two doses of the vaccine at different intervals (1, 2 and 6 weeks). A blood test was taken to each child before the first dose was given and two weeks after giving the second dose. These samples were sent to the United States for processing.

#### D. SCHEDULE OF ACTIVITIES CARRIED OUT

On 14 October, Dr. Ricardo Bustamante traveled to Washington D.C., invited by the PAHO to attend a meeting whose object was to analyze the different projects evaluating vaccines against cholera in Latin American countries, the area where the experiment that is being undertaken in Iquique by a work team from the W.R.A.I.R, headed by Dr. Robert A. Kuschner is inserted.

On 7 November Dr. Patricia Gassibe came to our Laboratory to inform us that she would be in charge of the Research Project into Meningococcal Disease. The first project concluded on 31 June 1991, and on 20 September a new cooperation agreement between the U.S. Army Medical Research Acquisition Activity and the Chilean Ministry of Health was commenced, through the Pan-American Health Organization (Appendix 7).

On 13 November Dr. Kuschner confirmed that vaccination against Cholera in Iquique will begin.

Between 22 and 24 November, the nurse Mrs. Marcela Martínez and Dr. Ricardo Bustamante met with the Municipal authorities of Colchane in the Altiplano in order to coordinate the study of pharyngeal carriers of meningococcus in the sector of Cariquima. With the help of new funds from Santiago coming from the cooperation agreement, this stage of the control was authorized to begin. (Appendix 5A)

Mrs. Marcela Martínez, the project nurse, trained students in an Nurse's Aides course on Epidemiological Surveillance.

A letter of consent to be signed by the parents of the children included in the vaccination against cholera was drafted in Spanish in the United States. This was sent to Santiago on 14 November for revision. In Santiago it was written in different terms by the Ministry of Health for its better understanding.

Between 5 and 7 December, Drs. W. Zollinger and R. Kuschner arrived in Iquique accompanied by Drs. Patricia Gassibe and Jorge Toro. This time they evaluated the work done at our Laboratory and the work schedule for 1992 was defined. On the basis of what was discussed then, a budget covering the period January through August 1992 was sent on 30 December, which included the expenses to be incurred during the cholera vaccination program while maintaining surveillance on meningococcal meningitis. This was subsequently analyzed then approved by the team from the Ministry of Health.

Between 11 and 14 December, a work team in charge of the Laboratory for Research into Meningococcal Diseases traveled to Cariquima for carrying out the control study of pharyngeal carriers. The samples thus taken were sent to the Public Health Institute for determining the presence of the meningococcus group and serotype.

Between 17 December and 14 January several meetings were held to inform the parents of children under 15 and over 2 years of age about the vaccine against cholera, in order to obtain their cooperation, apart from coordinating meetings and training the personnel who was going to work on the different activities included in this study.

On 20 January the vaccination control study against cholera began, which continued without interruption in its first stage until 27 March. The next stage will be done in August of this year.

Yours faithfully,

Marcela Martínez

Dr. Ricardo Bustamante R.

Distribution:

Dr. Patricia Gassibe / Ministry of Health  
Dr. Ramses Aguirre / Iquique Health Service  
Dr. Robert Kushner / WRAIR  
Dr. Antonio Marino / Regional Health Services  
Dr. Gustavo Mora / OPS in Chile  
Dr. Mateo Budinic / Ministry of Health  
Dr. Lorian Castillo / Public Health Institute  
Dr. Luis Martínez / Ministry of Health  
Dr. Gastón Paves / Pediatrics  
Dr. Ricardo Bustamante / Project  
Mrs. Marcela Martínez / Project  
File  
Dr. Jorge Toro.

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\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
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Laboratory for Research  
into Meningitis - Cholera

Iquique, 1 July, 1992

REPORT ON ACTIVITIES  
APRIL 1992 - JUNE 1992

MENINGOCOCCAL INFECTION SURVEILLANCE

Once the anti-cholera vaccination stage had finished, active surveillance of all meningococcal infections continued. Until March of this year, the number of confirmed cases was similar to that of last year at the same date, but from April onwards there was a steady increase in them; noteworthy was the fact that with an interval of two weeks between one case and the other, there appeared three meningococcemias in children aged under two; two of them were cousins who visited each other fairly frequently and the third with no special ties with the other two. Unfortunately all died. Up to this date we have recorded 18 meningococcal infections, 4 of them in adults (table 1).

The same time last year only 8 confirmed cases had been recorded and one highly suspect, without deaths. This situation is shown in the graphs in Appendix 8.

The meningococcemias, all dead, which appeared in April, gave rise to an evaluation with regard to meningococcal infection in the city, insisting on the possibility of early diagnosis at a clinical level, also reinforcing the work of the medical technicians in the Laboratory (covering 18 hours daily).

The recording of cases of meningitis, their etiology and distribution according to age during the period January through June 1992 is as follows:

<u>ETIOLOGY</u>	<u>N° of cases</u>
Neisseria meningitidis	18
Haemophilus influenzae	02
Streptococcus pneumoniae	02
TBC	01
Viral	02
Non identifiable germ	05

Neisseria meningitidis

<u>AGES</u>	<u>N° of cases</u>
1 year of age and less	03
≥ 2 years and ( 5 years of age	06
≥ 6 years and ( 14 years of age	05
≥ 15 years and ( 20 years of age	01
> 20 years of age	03
Total number of cases	18

Fifty percent of the cases appeared in children under five years of age; approximately 30% of those children's contacts were nasopharyngeal carriers of Neisseria meningitidis, and were mainly adults.

The geographic distribution within the city has been reduced to three well defined sectors where there is a high population density and poor sanitation and housing which is consistent with the conditions described as being environmental factors favorable to the spread of the meningococcal infection.

TABLE 1

CASES OF MENINGOCOCCAL INFECTION      IQUIQUE      JANUARY-JUNE 1992

CASE

Nº

DATE ADMITTED

GIVEN NAME

FATHER'S NAME

MOTHER'S NAME

AGE

YRS

DIAGNOSIS

EVOLUTION

Meningococcic meningitis

D/H (discharged healthy)

Dead

## SCHEDULE OF ACTIVITIES

At the end of April and through the hospital management, professionals from different clinical services of the hospital were summoned in order to brief them on the situation regarding the meningococcal disease in Iquique and put before them a working plan to try to curb the outbreak of this disease (Appendix 1).

The same summons was sent to the municipal outpatient clinics (Appendix 2).

Initial interest was very low in the beginning, except for a group in Pediatrics with whom a meeting was held, and for the nurses and two doctors from outpatient clinics in the outskirts of Iquique. On that same date we requested the Director of Health Services to order the taking of pharyngeal smears from contacts of patients with meningococcal infection prior to routine chemoprophylaxis. This is done with the object of making a more direct evaluation of the healthy carriers of meningococcus in the pharynx, because making a larger study of nasopharyngeal carriers would mean high costs, the difficulty of carrying it out and doubtful results (Appendix 3),

On 6 May 1992, the team met with Dr. Ramses Aguirre, the Director of the Iquique Health Service in order to inform him of the present situation regarding meningococcal meningitis in the city and propose a work plan (Appendix 4).

On the basis of what was discussed, it was decided to prepare a definition of the costs of a pharyngeal smear in case private groups request it from the Service (Appendix 5).

We also requested that information be reinforced at a hospital level regarding the present situation of the meningococcal infection. It was decided that pharyngeal smears would be routinely carried out prior to chemoprophylaxis in all contacts of patients with meningococcal infection, according to what was discussed previously and which was first put into action from 10 June 1992 onwards.

On 29 April a request was received from the Children's Home belonging to the police force for carrying out preventive examinations of meningococcal infection there (Appendix 6).

A total of 81 pharyngeal smears were taken, 18 of which were positive for *Neisseria meningitidis* (Appendix 7).

All positive cases were taken a control smear a month later which still showed two positive cases. Considering the possibility that these persons could have been reinfected by their respective families, their relatives are also taken pharyngeal smears. So as to rule out any resistance of the meningococcus to Rifampin, the children who's smears continued to be positive were once more given treatment, with control smears 24 hours after the treatment was over.

With the outbreak of three cases of meningococcal meningitis in adults in the first week of June, a meeting was convened with the director, head of the Persons' Programs and the Iquique Health Service nurse in order to decide what action was to be taken, submitting all the pertinent information that this laboratory possesses (Appendix 8).

It was proposed to:

1. Reinforce the prevention campaign and information to the community by the Iquique Health Service.
2. Clearly define how to handle contacts of patients suffering from meningitis, carry out immediate notification of any cases; widen criteria regarding contacts and take pharyngeal smears from them.

It was decided that the medicine to be used for the eradication treatment of meningococcus in healthy pharyngeal carriers would be Ciprofloxacin in doses of 750 mg. for one time in adults (during home calls we verified that there was a large number of adults who abandoned treatment with Rifampin during four days), and Rifampin during two days to children younger than 15 years of age in doses of 20 mg/kg of weight/day.

The Public Health Institute was asked to verify the minimum concentration of Rifampin necessary for inhibiting development of *Neisseria meningitidis*.

3. Define those groups most at risk and educate them regarding this disease (Appendix 9).

## ANTI-CHOLERA VACCINE PROJECT

On 3 August the second and final stage of evaluation of the anti-cholera vaccine will begin. This stage consists of administering a booster dose and taking blood samples from the volunteers who took part in the first stage. For this reason, the verification of addresses, schools and kindergartens where these youngsters attend has begun so that they are easier to trace when the date comes around (Appendix 10).

The teams and the dates of administration of the booster doses are put together in the different places where it will take place. (Appendix 12)

Between 5 and 7 July, briefing meetings were held with the parents of the volunteer youngsters regarding this last phase.

The PAHO was requested for funds for starting to disseminate this activity during the month of July, the costs for which are included in the budget submitted for the period January through August 1992.

## ADMINISTRATIVE AND FINANCIAL SITUATION

During this year, given the low incidence of meningococcal infections in Iquique compared with previous years and due to having only one epidemiological surveillance program of these infections going, it was decided to reduce the work hours of the employees of this laboratory according to what was set out in the previous report regarding activities. Nevertheless, due to the fact that during the month of August another phase of the anti-cholera vaccine project will be completed and which, according to previous experiences, needs exclusive and full time dedication, Dr. Jorge Toro has been requested to modify our contract to a full time one for the length of time this stage of the project lasts. This would include all medical, nursing and auxiliary-secretarial contracts (Appendix 11).

Funds available for the running of the laboratory during the period March through June have been used both for expenses for maintaining the laboratory and for other activities carried out. Accounts for the months of March, April and May, 1992 are attached. (Appendix 13)

To this date we have a balance of approximately CH\$ 100,000, and for this reason we are asking, through Dr. Jorge Toro, for the remittance of new funds of money from PAHO for expenses covering the last phase of the anti-cholera vaccine evaluation (Appendix 11).

There is no further information regarding activities between April and June 1992.

Yours faithfully,

Marcela Martínez Marco  
Project Nurse

Ricardo Bustamante Risco  
Medical Supervisor of Project

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\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
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Laboratory for Research  
into Meningococcic Meningitis

Iquique, 14 October, 1992

REPORT ON ACTIVITIES 1992  
FOR THE PERIOD JULY THROUGH SEPTEMBER

SURVEILLANCE OF MENINGOCOCCAL INFECTION

During the month of July this activity was continued with some modifications in the way it was being done. The aims of the surveillance were re-defined, with the following priorities:

1. To determine precisely the incidence of the meningococcal disease and the antigenic characteristics of the organism causing it.
2. To determine the feasibility of doing an efficacy test with a new and improved group B anti-meningococcal vaccine.
3. To evaluate a new polymerase chain-reaction method for detecting the presence of meningococcus in cerebrospinal fluid and serum.

During this period, nine more cases of meningococcal meningitis were bacteriologically confirmed, All of them were discharged in good general condition.

The etiological distribution during this year of bacterial meningitis infections is detailed in the following table:

<u>ETIOLOGY</u>	<u>N° of cases</u>
Neisseria meningitidis	27
Hemophilus influenzae	2
Streptococcus pneumoniae	3
Tuberculosis	1
Of unknown origin	8

This same situation is reflected in the following graph:

MENINGITIS 1992  
Bacterial Etiology

Cases

Etiology

Meningitis Laboratory

The distribution by ages and months of appearance of cases of confirmed meningococcal infection are shown in the following table:

As can be seen, 67% of all the cases were in children under 10 years of age, out of whom 78% were under five.

The present rate is 17.7 cases / 100,000 inhabitants.

The mortality rate for this year stands at 14.8%, exclusively derived from four cases of meningococcemia which evolved rapidly, even though they were diagnosed and treated at an early stage. Taking this group into account (5 cases in total), mortality here was 80% (Appendix 1).

Overall mortality of meningococcal infections during the epidemiological surveillance period of 1987 - 1992 was 7.5%.

During 1992, three secondary cases have surfaced with periods of appearance of the disease that go from 4 to 35 days, after the index case. All of them appeared in youngsters that had not received the prophylaxis with Rifampin, and were relatives who did not live in the same home of the index case but visited frequently.

This obliged us to rethink the way contacts are handled, widening the title of contacts to also cover those who although not living under the same roof as the patient, maintain regular contact with him/her.

With reference to this same situation, a meeting was convened with Dr. Miriam Escobar, Head of the Department of the Persons' Program of Iquique for Health Services in Iquique; Mrs. Leandra Grawe, a nurse from the same department; Dr. Gaston Paves, Head of the Pediatric Service of the local Hospital and the nurse belonging to the project, in order to review the situation regarding the meningococcal disease this year in Iquique.

This time, guidelines for the work proposed by the Laboratory were reviewed, which consist of continuing taking samples for pharyngeal smears from the contacts of the patients with the meningococcal disease, because the group evaluated up to this moment is small and in order to witness any important variation in the population with regard to pharyngeal carriers of meningococcus that might produce a greater increase in cases of the meningococcal disease (Appendix 2). This smear would now be accompanied by immediate chemoprophylaxis when dealing with contacts living under the same roof and in accordance with the result of the smear in the case of classmates or work colleagues.

Up to this moment, 453 pharyngeal smears have been carried out in relatives of persons ill with meningococcal meningitis, in some contacts in the work place, in playmates in the same course in the kindergarten and in neighbors or friends who have kept up more or less frequent contact.

The carriers found up to this moment are 18% for *Neisseria meningitidis*, and if restricted to the epidemic strain, this then falls to 1.1%. These figures are similar to those obtained in the sampling carried out in 1987 among 1,017 school children, although the group we are now working with is considered as of the highest risk.

Even though there has been an increase in the number of cases compared to 1991, according to the reports issued by the Public Health Institute, changes have not occurred in the infecting strain which continues to be group B, serotype 15, sup-type 1.3 This still has to be confirmed by the W.R.A.I.R. (Appendix 3)

## PHASE II OF THE ANTI-CHOLERA VACCINE PROJECT

The last stage of evaluating the anti-cholera vaccine was carried out between 3 and 31 August. Of the 485 initial volunteers, the evaluation was able to finish with 408 of them.

This stage included a booster dose of the oral vaccine, with a blood sample immediately thereafter and a second blood test 15 days after the first (Appendices 4, 5 and 6).

For concluding this stage we had the valuable cooperation of the Health Service and Municipal Corporation, with nurses from those entities taking part, as well as students from the nurse's aides course. We also had drivers and vehicles from the Iquique Health Service who were of great help in transferring all the equipment to the different work places (Appendix 6A).

From the United States came Drs. Kuschner, Andrew Trofa, Konrad Hayashi and the medical laboratory technician Higinio González, who carried out several activities during this period.

In September all the serum samples were sent to Dr. Ann Mari Svennerholm at the University of Gotheberg in Sweden, who is in charge of determining the antibodies and vibriocide activity in these samples (Appendix 8).

The final results of this study will probably be available by the end of the year, at which time the volunteers who participated will be also be informed.

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Laboratory for Research  
into Meningococcal Disease

## REPORT ON ACTIVITIES MAY - AUGUST 1993

### Epidemiological Surveillance

During this period the distribution of new cases of the meningococcal disease was as follows:

	Confirmed Cases	Suspected Cases
MAY	0	1
JUNE	1	0
JULY	4	4
AUGUST	1	1

Of the six confirmed cases, 4 were children under three years of age and the other two a child of 11 and a young girl of 15.

Worthy of note was that the four cases reported in July all appeared in the space of three days, during the last week of the month; 14 days after the religious holiday of "La Tirana", without there being any link between them. Two of the children had attended the festival but there did not exist any link between them and the other two who had stayed in the city.

Of the cases reported as suspected in July there was a link between two of them within a space of 18 days between one case and the other. In both cases a pharyngeal smear was taken from the contacts, 16 in total, all being negative for *Neisseria meningitidis*. The other two suspected cases were not linked in any way neither with those already mentioned above; the brother of one of these cases was a carrier of meningococcus and he was given the eradication treatment. Thirty-four contacts of this group of persons suspected of having the meningococcal disease were examined, with one sole case of a pharyngeal carrier of meningococcus being found.

Distribution of the meningococcal infection according to etiology:

	MAY	JUNE	JULY	AUGUST
Meningococcus	0	1	4	1
TBC	0	1	0	0
S. pneumoniae	0	1	2	0
Viral	2	1	1	4
H. influenzae	0	0	0	1
Streptococcus B	0	1	0	0

There were no deaths from the infections of meningococcal etiology. The sole case of TBC died, also the one who had group B Streptococcus (newly born), and one of the cases of Pneumococcic meningitis (a baby under 12 months old).

The cases recorded as viral etiology were based on the characteristics of the cytochemistry of the CSF and its benign evolution, without the help of antibiotics, that each of them showed. In relation to these cases in the month of July it is important to point out that two of them were brothers and the other two were classmates.

In the four cases of viral etiology in July a control of the contacts was made, including the pupils attending the same course as the two ill students, without finding any pharyngeal carriers of meningococcus. In this group a total of 74 cultures of pharyngeal secretion for Neisseria meningitidis were taken.

The total distribution of the cases of meningococcal disease by ages for the first eight months of 1993 is as follows:

MENINGOCOCCAL DISEASE  
Iquique 1993 (Distribution by age)

Age Ranges

It appears that the tendency is always towards groups of children, 57% of the cases being children of between one and four years of age. If we also include children between 5 and 9 years of age, altogether they account for 78.6% of all the cases for this year. There were no cases over 15 years of age.

When comparing the incidence of meningococcal meningitis in 1993 with 1992 the following graph is obtained:

MENINGOCOCCAL DISEASE  
in Iquique, comparing 1992 with 1993

The monthly distribution has had important differences in some months; the rate up to August 1993 being significantly lower (7.8 / 100,000) than that of the same period in 1992 (14.9/100,000). Nevertheless, the mortality rate was higher in 1993, 23.1% as opposed to 16%; occurring in both years (with the exception of one case) in children under three years of age.

Laboratory Activities

In May, faced with the admission of new health professionals to the different levels of health care in our city, the bibliography, norms and procedure regarding epidemiological surveillance of the meningococcal disease were sent to the Department for Primary Care of the local Health Services and to outpatient clinics in the surroundings. Added to this, a meeting was held to inform a group made up of a mixed commission from education and health departments at the outpatient clinic level regarding Meningitis in Iquique.

With our support the local Hospital prepared an information sheet addressed to all parents who come with their children

looking for medical care from the Emergency Services, and in whom a fever condition of a non-defined etiology would have been found in order to be on maximum alert in the event of the outbreak of a meningococcal infection in the early stages from a clinical point of view.

At the end of May, information regarding our activities and ways we could help the Heads of the Department of Persons' Program so that this department could program educational activities based on our proposal.

In this same period we received a visit from Dr. Patricia Gassibe who, although she was in the city for other reasons linked to the local Health Service, took the advantage of reviewing our activities up to this moment and she suggested some guidelines in relation to the analysis that we were doing in the records we had at our disposal.

In June all those contacts of patients with meningococcal disease who had been diagnosed to be pharyngeal carriers of meningococcus and who had received treatment met together in order to evaluate their condition as carriers after 6 months and one year after the eradication treatment. The preliminary results show that the presence of meningococcus in the pharynx in this group has been low, approximately 5.9% for group B N. meningitidis and only 1.2% for the epidemic strain. It was decided to continue evaluating these patients until the end of the year when we will hand in a complete report.

In July, faced with the visit of Drs. Kuschner and Zollinger to our country, the work teams in Antofagasta and Iquique met in the former of the two cities in the presence also of the principal researcher, Dr. Jorge Toro. This meeting was arranged in order to supervise all activities carried out up to that moment, to define some common work plans for both cities, look into the feasibility of funding some local activities attached to the same epidemiological surveillance plan and to obtain information on the present situation of research into the anti-meningococcal vaccine that is being carried out at WRAIR.

In August an invitation was sent by the Minister of Health, Dr. Julio Montt to Dr. Bustamante to attend an informative meeting regarding the latest in relation to a Cuban anti-meningococcal vaccine. At that time, Dr. Bustamante also assisted on the deliberating committee regarding the application of this vaccine in our country.

### Administrative and Financial Aspects

Constant contact has been kept up between the team working in our Laboratory, with periodic meetings (every three months) in order to fine-tune details or make changes in our internal working methodology.

There is a constant monthly interchange with the team in Antofagasta in all that refers to new epidemiological information arising in both cities and to several aspects linked to our jobs in general.

The maintenance of our Laboratory regarding daily expenses needed for replacing materials as well as maintaining equipment, has been solved for the time being by the Health Service in Iquique.

The expenses we have incurred up to this date which only include the preparing of slides for the educational program concerning meningococcal meningitis as an extra, less all discounts corresponding to contributions made by PAHO/WHO, stand at CH\$ 902,812.- (See Appendix)

Yours faithfully,

Marcela Martínez Marco  
Project Nurse

Dr. Ricardo Bustamante Risco  
Project Supervisor

with copy to:

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REPORT ON THE ACTIVITIES OF THE LABORATORY  
RESEARCHING INTO THE MENINGOCOCCAL DISEASE

Period September - December 1993

Epidemiological Surveillance

During this period we opened thirteen new records, only one showing bacteriological confirmation of meningococcal infection which corresponded to a fatal meningococcemia; two cases were highly suspected of meningococcal with isolation of *Neisseria meningitidis* only in the culture of pharyngeal secretion. The following table shows the etiological distribution of the cases recorded during the last four-month period of 1993:

Etiology	N° of cases
N. meningitidis	1
Type B haemophilus inf.	3
S. pneumoniae	1
Viral	3
Unknown	4
Others	1

In the meningitis classified as viral, we do not have either the means or the experience for virological studies, however the clinical aspect, biochemical analysis of the CSF and the evolution of the patients were all clearly indicative of this etiology. In others there is one classified as meningism.

A review of all the cases of meningococcal infection in 1993 shows us a significant decrease in the rate of incidence when compared to the previous year: 9.56 cases x 100,000 inhabitants from the whole province and 10.48 cases x 100,000 inhabitants for the municipality of Iquique.

Mortality underwent a sharp increase compared to the figures for previous years, standing at 25%. This was caused by meningococcemias, with the death of four out of the five cases.

(Iquique has, according to the latest census, 167,243 inhabitants in the province and 152,589 in the city.)

The following table shows the etiological distribution of all cases of meningococcal infection recorded during 1993 in Iquique.

<u>Etiology</u>	<u>N° of cases</u>
N. meningitidis	14
TBC	2
Type B haemophilus inf.	4
S. pneumoniae	4
Viral	12
Unknown	13
Streptococcus group B	1
Others	3
<hr/> TOTAL	<hr/> 53

Of special significance is the high number of processes in which the germ could not be identified, because this then leaves us with a considerable number of cases which potentially could be meningococcal infections; something which would significantly change the rate of outbreaks in Iquique.

Type B Haemophilus influenzae has gained an increasing relative importance as the cases caused by meningococcus decrease, experiencing a slight increase in the number when compared to the last two years.

Under the heading "Others" are included the cases in which a meningitis infection was suspected initially, but rejected later.

In the 14 cases in which there was bacteriological confirmation of meningococcus, this was carried out in an CSF culture, and only four of them showed positive hemocultures also, and in 7 cases the germ was isolated in a culture of pharyngeal secretion. To this should be added that Neisseria meningitidis was also isolated in cultures of pharyngeal secretion in one case of pneumococcal meningitis, in one case of viral encephalitis and in three cases that were classified as being highly suspected of carrying the meningococcal infection.

The age distribution of the highly suspect and confirmed cases of meningococcal meningitis was as follows:

Age Range	N° of cases	%	Accumulated
< 1 year old	1	6.3	6.3
1 to 4 years of age	9	56.3	62.5
5 to 9 years of age	4	25.0	87.5
10 to 14 years of age	1	6.3	93.8
15 to 19 years of age	1	6.3	100.0
20 to 24 years of age	0	0.0	0.0
25 to 29 years of age	0	0.0	0.0
30 years of age and over	0	0.0	0.0
TOTAL	16	100.0	

It can be easily appreciated that 62.5% of all cases are found in children under 5 years old, the mortality rate being exclusive to that age group which, if we calculate it exclusively for cases that appear in this age range, reaches 40%.

Eighty-one point two percent of all cases appeared between 1 and 9 years of age with a mortality rate of 23% for this group.

Regarding diagnoses, 31.3% of all cases appeared as meningococcemia. Of them it must be mentioned that, although N. meningitidis was isolated in all the CSF cultures, in two of them the cytochemical analysis of this fluid was totally normal, without alteration of glucose, proteins or the presence of leucocytes.

In 87.5% of all cases, the diagnosis was made within 24 hours of symptoms appearing. The remaining 12.5% were diagnosed within 48 hours.

## Laboratory Activities

In October 1992 our team was invited by the Sub-Region for Health of Tacna to an "International Seminar and Workshop on the Prevention, Surveillance and Detection of Meningitis". This event was attended by the nurse, the medical laboratory technician and the doctor supervising the project, who gave presentations in their own fields. This time we were also able to share our experiences with two consultants of the PAHO in Peru.

At the end of the same month, Dr. Bustamante attended the II Chilean Congress on Epidemiology held in Santiago, taking part also in one of the pre-congress courses.

Also in October we did a survey which measured the perception that the community has regarding information on meningococcal meningitis and which were the channels of communication they used. For this purpose 90 inquiries were made to the parents of 3 kindergartens and two schools covering the whole social spectrum from top to bottom in Iquique.

The results obtained showed that the principal channel of information is television and that the majority are of the opinion that information on meningitis is clear but incomplete, with questions which were not always answered by the persons polled.

Taking advantage of this survey, informative talks were given to the persons polled in relation to meningococcal infection in Iquique and the rest of the country.

At the end of November, Dr. Bustamante was invited to take part as speaker in the "VII Chilean Conference on Public Health" sponsored by the Chilean Society for Public Health.

At the end of September the Medical laboratory technician Mr. Fermín Mendez A. attended a "Training Course on the Laboratory Diagnosis of Neisseria meningitidis".

In November the taking of cultures of pharyngeal secretions from the contacts of patients confirmed or suspected of having meningococcal infection was completed. This was done with the object of evaluating pharyngeal carriers of meningococcus in the sector of the population which is at greatest risk, the efficacy of chemoprophylaxis and the frequency of pharyngeal reinfection which occurs in this sector of the population. The results from this study will be sent later.

### Administrative and Financial Situation

The work team at this Laboratory has remained stable during the last four-month period of the year.

In November, the contribution from WHO/PAHO for CH\$ 902,813 was sent to the Health Service in Iquique in order to cover accumulated debts with this Service up to 31 August 1993.

According to the latest balance sent by the Health Service, up to 31 November, they are owed CH\$ 263,227.

Marcela Martínez Marco  
Project Nurse  
Iquique, February 1994

Ricardo Bustamante Risco  
Doctor Supervising Project

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LABORATORY RESEARCH INTO THE MENINGOCOCCAL DISEASE  
IQUIQUE 1994

PERIOD JANUARY - AUGUST 1994

Epidemiological Surveillance

From 1 January to 31 August 1994, we have recorded 6 cases of the meningococcal disease in Iquique with a rate for that period of 3.58 per 100,000 inhabitants. By the same date in 1993 we had recorded 13 cases with a rate of 8.03 per 100,000 inhabitants. Graph 1

MENINGOCOCCAL DISEASE  
JANUARY THROUGH AUGUST 1993-94

The average weekly number of cases amounts to 0.17, and this stood at 0.37 in 1993. Compared with 1993, in which there was a concentration of cases between weeks numbers 9 and 14 and then again in week number 31, this year we have only had a slight accumulation in weeks 31 and 33.

It is then clearly evident that there is a decline in the number of cases of meningococcal disease in our city, although it is still early to give just one reason for it. Among the factors that must be born in mind for this decline, are the following:

1. The natural evolution of the epidemic curve
2. A depletion in susceptible persons due to continuous exposure to the meningococcus
3. Excellent coverage when handling contacts
4. Great efficacy of the chemoprophylaxis given at a local level in eradicating the meningococcus from pharyngeal carriers.

Five of the cases that we have had this year have been dwellers of the city of Iquique, with one sole case coming from Pica, an oasis located on the lower reaches of the Andes 120 kilometers from Iquique. No new cases have arisen in this township after six months have passed since this sole case was detected in the sector.

### Description of Cases

All the cases appearing this year have been aged 7 or under, and of these only two were less than 5 years of age (28.5%). Graph 2.

#### MENINGOCOCCAL DISEASE AGE RANGE 1994

Range of Age	N° Cases	%	Accumulated
< 1 year old	0	0	0
1 to 4 years of age	2	33.3	33.3
5 to 9 years of age	4	66.6	100

#### Meningococcal Laboratory Iquique 1994

None of the 1994 cases died, and only one case had serious muscular-cutaneous consequences in the legs derived from a meningococcemia with a Waterhouse-Fredericksen syndrome.

In all the cases, consultation was made and diagnosis suspected within 24 hours of symptoms beginning, except in one case in which, although the patient was hospitalized, the signs only started appearing 18 hours after admission.

The etiologies found in all the cases of meningitis recorded during this year in our city are shown in the following table:

#### MENINGITIS Etiological distribution (1994)

<u>Etiology</u>	<u>N° of cases</u>
N. meningitidis	6
Type B H. influenzae	1
S. pneumoniae	4
Group B streptococcus	2
Group A streptococcus	1
Viral	3
Unknown	4
Meningococcal Laboratory Iquique 1994	

## Laboratory Activities

Once the collection of samples for cultures from pharyngeal secretions up to November 1993 had concluded, during the first four months of this year we started sorting all the data obtained for its subsequent analysis. We prepared a report that was presented during the III Conference on Public Health in the Northern Regions which takes place annually in the city of Copiapó. This year the event took place between 24 and 26 August. Appendix 1.

In the month of May, Dr. Bustamante attended a workshop called "Stratifying Risk Factors of Transmissible Diseases" organized by Dr. Carlos Castillo Salgado, Regional Adviser in Epidemiology of the Pan-American Health Organization. Appendix 2.

At this point in time we are reviewing all the confirmed and highly suspect cases of meningococcal disease that we have held in our records since 1987. What we are doing is trying to carry out an exhaustive review of the epidemiological behavior of this illness in our city over the past seven years.

## Administration and Finance

Our staff at present in the Laboratory is made up as follows:

1. Supervising Doctor (1)
2. Nurse to support the Project (1)
3. Medical laboratory technician (1)
4. Auxiliary Secretary (1)

Each one's activity has remained unaltered throughout the year, doing their four-monthly scheduled duties and will continue so until the end of this year.

Expenses incurred have been restricted almost exclusively to maintaining the Laboratory, considering basic items, stationery, cleaning material and maintenance of equipment.

In Appendices, photocopies are attached of the five expense sheets from our Laboratory sent by the Health Service of Iquique. Up to this date, we have not obtained more updated information regarding our expenses from the Service, and so the reimbursement of \$ 553,571 made by PAHO in May of this year (see appendices) as well as the charge of \$ 329,691 for electricity corresponding to

the period June 1993 through May 1994 made by the Hospital and which had not been previously charged, do not appear in these figures. (see Appendices).

Marcela Martínez Marco  
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Project Supervisor for Meningitis

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Dr. Ricardo Godoy / Regional Health Service for the 1<sup>st</sup> Region

Dr. Wendell D. Zollinger / WRAIR

EPIDEMIOLOGICAL SURVEILLANCE NORMS

ON

MENINGOCOCCAL MENINGITIS

1993

Meningitis Laboratory Iquique

EPIDEMIOLOGICAL SURVEILLANCE NORMS  
MENINGOCOCCAL MENINGITIS  
IQUIQUE

Case Classification

- 1- CONFIRMED : Isolation of Neisseria meningitidis from CSF or blood or a Gram tinction consistent with N. meningitidis.
- 2- SUSPECTED : With a set of signs and symptoms consistent with meningococcal infection but with no laboratory findings.
- 3- CONTACT : Persons who live and sleep under the same roof and those who have had direct contact with the patient (kisses on the mouth or who have been in direct contact with the patient's saliva within a period of 10 days prior to the diagnosis).

Case Handling

All persons who are admitted to a hospital or a clinic with a diagnosis of Meningitis or a suspected set of signs and symptoms will be subject to the following examinations:

- 1- CSF : The best method is to take the minimum amount of 1 cc and split it between two sterile tubes. One for the cytochemical exam and the other for a bacteriological exam.  
(Place a little in a vial for freezing in the Meningitis Laboratory on the 6<sup>th</sup> Floor).
- 2- QRCP (Quantitative Reactive C Protein): Is evaluated from the blood serum and the amount taken depends on the local laboratory.
- 3- PHARYNGEAL SECRETION: For isolating Neisseria meningitidis. The best method is the Thayer Martin one.
- 4- ACUTE SERUM : 2-8 ml of blood taken within the first 24 hours of admittance of patient or at the time in which the diagnosis is suspected and then 18 to 20 days after admittance, the CONVALESCENCE SERUM is taken.
- 5- HEMOCULTURE

6- HEMOGRAM - ESR or any other exam the doctor considers necessary.

### Laboratory Activities

During these first four months of the year, the team nurse compiled all cases defined as confirmed and highly suspected of having meningitis since 1987 up to December 1992 that we have on record and which are included in the official information we have available. The reason for compiling this was to define the basic and general epidemiological aspects of each patient, without including the clinical data as yet. Through this work we have been able to make an initial evaluation in relation to greater incidence of this disease by sex, age range, geographic distribution, the final condition of each one of the cases, seasonal and monthly distribution, mortality and others which require a more exhaustive analysis for formal submission.

Concurrently and so as to get a profile and measure the efficacy of the chemoprophylaxis in contacts, apart from widening coverage for them, double pharyngeal smears have been taken prior to the prophylaxis and immediately after it in those cases where the presence of *Neisseria meningitidis* is verified. In June of this year, we celebrated our first anniversary with this work, with medium-term smears still to be taken from those cases who were positive in the first sample. For this purpose, this activity was scheduled to include summoning all contacts and index cases who showed they were pharyngeal carriers of meningococcus. Once this is completed we will begin to tabulate all the data for its subsequent evaluation.

It should be mentioned that this will allow us also to quantify the efficacy of Ciprofloxacin in the eradication of pharyngeal meningococcus and compare it with that of the Rifampin that had been, up to October of last year, the only medicine used in chemoprophylaxis (refer to the October-December 1992 report).

## Cholera Project Activities

According to what is stipulated in the protocol of the evaluation of an anti-cholera vaccine which was given to volunteers aged 2 to 15 in Iquique between January and August 1992, this also includes the administration of the vaccine to the placebo group once its efficacy and lack of side-effects has been verified.

This activity was carried out between 11 and 29 January, administering the vaccine in the doses that had been administered to the initial study group with an interval of one week between one dose and the next. This was decided due to the fact that the efficacy, so far as the generation of antibodies is concerned, was equally significant for the study group in the interval of 1 and 2 weeks between doses, and less significant, when the interval was stretched to 6 weeks.

Of the 103 volunteers in the placebo group, 47 of them received the first dose and of these 18 came to get their second dose. None of them were followed up, although they were warned that in the event of any ill-feeling they were to consult us. In August of this year this same group of volunteers was administered a booster dose.

We do not have the latest data in Iquique regarding the analysis before and after the booster dose which was given to the volunteers incorporated in the evaluation of this vaccine carried out in August 1992.

Administrative and financial aspects

Expenses incurred in the maintenance of the Laboratory during the first four months of the year have been covered with the contributions of the Iquique Health Service; this sum, which amounted to Ch\$ 293, 729, has been recently reimbursed by the PAHO.

The other significant additional expense was the preparation of audiovisual aids for use in education and also to give to the local Health Service when requested.

The development of activities connected to the surveillance such as studying the development of contacts of index cases and reviewing and evaluating all the confirmed cases kept in our records since 1987 has given us more work on a daily basis but which have been done without any delays.

Yours faithfully,

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Project Nurse

Ricardo Bustamante Risco  
Project Supervisor

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Dr. Gustavo A. Mora	/ PAHO/WHO in Chile
Dr. Ramses Aguirre M.	/ Health Services Iquique
Dr. Gastón Paves Ulsen	/ Health Services Iquique
Dr. Miriam Escobar	/ Health Services Iquique
Dr. Antonio Marino M.	/ Regional Health Services 1 <sup>st</sup> Region
Dr. Lorian Castillo	/ Public Health Institute
Mrs. Marcela Martínez M.	/ Project
Dr. Ricardo Bustamante	/ Project

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## MEASURES TO CONTROL THE PATIENT, THE CONTACTS AND THE PATIENT'S ENVIRONMENT

- 1- Immediately notify the DPP of the local Health Service by word of mouth and in writing (\* form RMC 14).
- 2- Isolate the patient for up to 48 hours after beginning chemotherapy.
- 3- Simultaneously disinfect the nasopharyngeal secretions.
- 4- Isolation measures: Of the respiratory type. Norms attached.
- 5- If the patient is in fact a pharyngeal carrier of meningococcus, he/she must receive chemoprophylaxis before being discharged from the hospital or the clinic after the primary infection has been treated. Pharyngeal meningococcus is only eradicated by treating with Rifampin and Ciprofloxacin.

## CONTACTS

- 1- Once the data has been received, the nurse of the outpatient clinic in the area of the patient's home must make an epidemiological home call on the contacts within 12 hours.  
In the cases of meningococcal meningitis, contacts are all persons who:
  - Sleep under the same roof either permanently or temporarily.
  - Have been living for at least 7 to 10 days beforehand in the home of the patient.
  - Have maintained direct contact with the patient in another home.
  - The concept of family group must be extended to include any member of the family who maintains a close and permanent link with the patient.
  - In the event the patient is being breast-fed or is a pre-schooler who attends a day care center or kindergarten, the children in the same room or level as the patient are also considered contacts.
  - If the patient comes from a children's home, regiment, orphanage or prison, the contacts must be defined according to the type of relationship they have had with the patient.
  - Hospital personnel, unless they have had any intimate contact with the patient, will not be considered as contacts. The same criterion is applied to companies, factories or offices.
  - For school children and university students, contacts are those who have had very direct relationships with the patient during the two weeks prior to the diagnosis of the disease.

## GENERAL ACTIVITIES

Owing to the presence in Iquique of a working group from the W.R.A.I.R during the month of August, Dr. Jeanette Vega, national adviser for the PAHO/WHO; Dr. Jorge Toro, Head of the Epidemiological Department of the Ministry of Health; Dr. Antonio Cárdenas, supervisor of the Meningitis Project in Antofagasta and Eduardo Araya, chief accountant of the PAHO/WHO in Chile arrived in the city.

The reason for this visit was to define working methods for our Laboratory on the technical side as well as to sort out its funding. Therefore, a report on activities which will take place during the period September through December in order to support the request for funds for that period was requested. Also, the monthly remittance of a report on our activities to Drs. Jorge Toro, Ramses Aguirre, Robert Kushner and Jeanette Vega was established. As far as this is possible, it should be sent during the first week of the month following the report.

All activities that Dr. Antonio Cárdenas has to do in Antofagasta as epidemiological surveillance supervisor of meningococcal infections in that city, were reviewed in detail. The possibility of rapid communication between Antofagasta and Iquique for any later consultations was established.

Dr. Robert Kushner informs that the new vaccine against Group B meningococcus is in phase I of evaluation in the United States. There have been minor delays at this stage because the highest dose that was being tested produced prolonged and moderately intense secondary effects in the place where the vaccine is injected. A reduced dose was tried which proved to have no ill effects. According to the results of this phase, phase II will be tried out in Antofagasta during the period March - April 1993.

Mrs. Marcela Martínez, the project nurse, met with Mrs. Maxi Ruz at the end of July to give her a detailed account of the activities that it is hoped Mrs. Ruz will carry out in Antofagasta as nurse for the Meningitis Project there.

Acting on the request of Dr. Felipe Otayza, director of the magazine "Demosalud" which is published and distributed by the Health Services of Iquique, Mrs. Marcela Martínez wrote an article about our activities in relation to the evaluation of an anti-cholera vaccine by our Laboratory (Appendix 13).

## SCHEDULE OF ACTIVITIES

In the month of July, the project nurse began the task of making contact again with the volunteers from the beginning of the year in the evaluation of an anti-cholera vaccine so as to work with them on the last stage to be carried out in August (Appendix 4).

Several meetings were held with the parents of those volunteers in the outpatient clinics in Iquique and also in the community of Alto Hospicio where approximately 40% of the samples had been taken.

On 30 July, Mrs. Maxi Ruz, the nurse working on the surveillance project of meningococcal infection which will begin in Antofagasta came to our Laboratory. The object of her visit was to get a feeling for the work she will carry out in Antofagasta shortly and in this she was helped by Mrs. Marcela Martínez.

On 3 August, administration of a booster dose of the anti-cholera vaccine began with volunteers who took part in the initial phase from January through March of this year (Appendix 7).

Unlike the first phase, this time the work took place mainly inside our Laboratory, with field visits for working in sectors like Alto Hospicio and Primeras Piedras and then later for recovering those volunteers who had lagged behind.

From 14 to 16 August we were visited in Iquique by Drs. Jeanette Vega, Jorge Toro, Antonio Cárdenas and Mr. Eduardo Araya.

On this occasion they dealt with aspects relating to the running of the Laboratory and the ways of obtaining financial contributions by the PAHO, which was also extended to the work which will be started in Antofagasta.

On 27 August Dr. Bustamante traveled to Santiago to attend the Conference on Therapies in Pediatrics which also included topics related to meningococcal meningitis and cholera. This time he took the opportunity of making contact with infectious disease physicians in Santiago (Appendix 11).

On 28 August the project for evaluating a Swedish-made anti-cholera vaccine which had been provided by a group of researchers from the W.R.A.I.R came to an end. Dr. Robert Kuschner, the researcher in charge of the project, together with Dr. Ricardo Bustamante, co-researcher, met with Dr. Miriam Escobar to make a formal presentation and to inform regarding the activities of the Laboratory relating to the anti-cholera vaccine as well as to the work of surveillance of meningococcal infections.

On 7 September, Dr. Miriam Escobar, through Mrs. Leandra Grawe, was given an update of the cases of meningococcal meningitis in Iquique during 1992, dividing them up into those with bacteriological confirmation and those which were only suspected but without laboratory confirmation (Appendix 14).

An estimate was prepared with a break down of activities of the laboratory personnel for the period September - December 1992 (Appendix 10).

On 9 September, samples of the serum obtained while evaluating an anti-cholera vaccine were sent to Dr. Ann Mari Svennerholm in Sweden. Confirmation of their safe receipt was received later on (Appendices 8 and 9).

On 14 September the results of the pharyngeal smears taken up to this date were tabulated and evaluated. These results were later evaluated by Dr. Miriam Escobar as part of the definition of activities to be done by the Health Service of Iquique in relation to meningococcal meningitis.

In 15 September, the second set of samples of serum from the anti-cholera vaccine project were sent to the United States, together with the records of each of the volunteers who took part. These were received without delay (Appendix 17).

In relation to a previous request for money to pay activities done by nurses who worked on the last stage of the anti-cholera vaccine study, on 17 September a check for CH\$ 260,000 was received from the PAHO (Appendix 12).

Dr. Escobar was sent the educational program for meningococcal meningitis addressed to community leaders of high risk sectors within the population of Iquique, for its analysis and discussion (Appendix 15).

Faced with the decision to continue with the pharyngeal smear samples from contacts of patients with the meningococcal disease, Dr. Kuschner's cooperation was requested on 22 September for obtaining culturettes and petri dishes; all essential items for this.

On 30 September in a meeting with Drs. Escobar, Paves, Mrs. Grawe and Mrs. Martínez, the handling of contacts of meningococcal patients was discussed, on the basis of what was proposed by our Laboratory. It is also confirmed that Dr. Bustamante will give a talk in relation to the past and present situation of meningococcal meningitis in Iquique, included in a course on Infectious Diseases and Immunology which will take place in Iquique between the 8 and 10 October. Invitations were sent to all physicians in Iquique, especially those who have only been a short time in the city (Appendix 16).

## ADMINISTRATIVE AND FINANCIAL SITUATION

With the visit from representatives of the PAHO/WHO in Chile, a better relationship was built up with them so that a series of aspects relating to financial and administrative management in this Laboratory could be explained.

Referring to the estimate sent for the period January through August, a correction was made in relation to the payment of hours worked during the month of August. In the initial estimate there were entries for four hours for that month which, due to the greater work load that the nurse, nurse's aide and the project physician all had, was later modified to full time (Appendix 18).

For the period September through December 1992, a new estimate was prepared based on what was discussed in a conversation with Mr. Araya, Dr. Vega (PAHO/WHO) and Dr. Toro (Ministry of Health) in which there were new headings for expenses not indicated in the previous estimate. Furthermore, a work schedule was added for this period which justifies the expenses incurred (Appendix 10).

It was insisted that all expenses to be incurred had to be duly backed with the relevant receipt, because the funds available are limited and must be shared with the the setting up of the epidemiological surveillance for Meningitis in Antofagasta.

During these last three months we have not had major difficulties concerning salaries and the funding of the project, thanks in a large measure to the positive attitude on the part of the PAHO and the Ministry of Health in that respect, as well as the cooperation rendered by the Health Service in Iquique. To this date we have a deficit in the funds available for the project in the Health Service in Iquique amounting to CH\$ 317,495. This was the result of additional expenses incurred during the month of August and subsequent purchases for replacing essential medical material and stationery which will be used during the rest of the year (Appendix 19).

## CONCLUSIONS

In general, our work at the Laboratory has been undertaken regularly without many obstacles in the way, having had a lot of activity in August due to the latest stage in the evaluation of the anti-cholera vaccine.

Later, we began to maintain a rigorous control of the new cases of meningococcal meningitis, maintaining close contact with the different entities of the Health Service in Iquique, which has been to our mutual benefit.

We wish to highlight that thanks to the PAHO and Ministry of Health we have received the proper support for our activities.

Yours faithfully,

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\*\*\*\*\*  
\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
\*\*\*\*\*

Laboratory for Research  
into Meningococcal Disease

## QUARTERLY REPORT OCTOBER - DECEMBER 1992

### Meningococcal Infection Surveillance

The last case of meningococcal meningitis for 1992 appeared at the end of November, nobody being admitted with a meningococcal infection in December. At the end of December a meningitis was admitted but it was not possible to isolate the germ that caused, but it did not appear to correspond to an infection by *Neisseria meningitidis*. A sample was preserved of the CSF from this patient for later analysis in the United States.

The following graphs show the situation in Iquique with respect to meningococcal infection during the year 1992, bearing in mind several variables.

The rate of incidence for this disease, which over the past two years had shown a downward trend, increased by about 50% compared to 1991 (Graph 1). It did not reach, however, the high rates experienced between the years 1983 and 1989.

Forty percent of the cases for this year were concentrated in the months of June through August, which coincides with a colder than normal Winter period in Iquique, something which normally results in greater overcrowding. In the rest of the months the distribution was more even, with the exception of December when there were no cases (Graph 2).

With respect to ages, 30% of all cases appeared in children between the ages of 5 and 14 and if we look at the overall incidence in all children of 14 years of age and under, this stands at 73.3% of the total number of cases confirmed (Graph 3).

Sixty-three of the cases were females and the ratio of women to men was 1.7:1 (Graph 4).

In relation to the mortality of meningococcal processes in 1992, there was an overall increase compared to 1991 (16.6% ;+2.3%;). If we restrict this mortality to children under 15 years of age, the figure increases significantly when compared to

the previous year (22.7% ;+6.1%;). This mortality was caused in all the cases by sudden outbreak of meningococemia even though there were no delays in diagnosing them.

GRAPH 2

MENINGOCOCCAL DISEASE  
Iquique January - December 1992

January  
February  
March  
April  
May  
June  
July  
August  
September  
October  
November  
December

N° of Cases

Meningitis Laboratory 93

GRAPH 3

MENINGOCOCCAL DISEASE  
Incidence by Month and Age (Iquique 1992)

Age Ranges

JAN  
FEB  
MAR  
APR  
MAY  
JUN  
JUL  
AUG  
SEP  
OCT  
NOV  
DEC

TOTAL

Meningitis Laboratory 93

DISTRIBUTION BY AGE AND SEX  
MENINGOCOCCAL INFECTIONS CONFIRMED BACTERIOLOGICALLY  
1992

	Females	Males	Total
< 1 year old	4	0	4
1 to 2 years old	2	3	5
3 to 4 years old	2	2	4
5 to 14 years old	6	3	9
15 to 24 years old	1	1	2
25 to 34 years old	1	2	3
≥ 35 years old	3	0	3
Total	19	11	30

## Activities

During this last quarter joint activities were carried out with the Persons' Program Department in order to define how all contacts with patients carrying the meningococcal disease are to be handled, receiving excellent cooperation from the nurses from three outlying outpatient clinics in Iquique to speed up and improve it.

In October, during a course on "Infectious Diseases and Immunology in Pediatrics", a talk was given by Dr. Ricardo Bustamante on the current situation regarding meningococcal diseases in the city and their evolution over the past five years.

This was accompanied by an insertion in a local newspaper explaining the same situation mentioned above. (Appendix 1)

During the month of October, telephone contact was established with Dr. Antonio Cardenas in Antofagasta for rendering him technical support in relation to the beginning of meningococcal infection surveillance in that city. He was sent some material from the Laboratory that they needed for this stage. Direct contact was maintained with the team in Antofagasta, both for exchanging opinions and also giving them our advice.

In November, the project nurse, Mrs. Marcela Martínez, gave training talks to auxiliary paramedic personnel related to epidemiological surveillance. At the end of this same month, she was invited to give classes on Basic Epidemiology to a course of auxiliary paramedic technicians in the course of 1992.

At the end of November, Dr. Bustamante met with Dr. Ramses Aguirre, the Director of Health Services in Iquique, to inform him of preliminary results of the evaluation of the anti-cholera vaccine carried out between January and August 1992. The administration of an anti-cholera vaccine to children inside the placebo group was defined with him, something that was contemplated in the working protocol and the parents of the volunteers were informed of this in a letter of consent which they all signed.

Through the Persons' Program Department, direct communication has been maintained with the Health Services in Iquique, giving them detailed information periodically relating to the appearance of any new cases of meningococcal infection that need to be recorded.

Between 8 and 10 December, our laboratory received the visit of Drs. Wendell Zollinger and Robert Kuschner who came to supervise our job. The work methodology was looked into and also surveillance on a large scale with the object of offering some ideas to the team in Antofagasta.

On this occasion it was decided we would be remitted some laboratory material that we needed, and which was eventually sent from Antofagasta in the middle of the month.

In accordance with the information provided in relation to classifying the germ in cases of meningococcal infection during 1992, there have been no variations in sero-group or sero-type in the epidemic strain that might explain the greater rate of incidence this year. Data from the W.R.A.I.R. is fully in agreement with that supplied by the Public Health Institute.

During the month of December, a working timetable was drawn up for administering the anti-cholera vaccine to the placebo study group carried out between January and August 1992. (Appendix 1 A). This activity will be done between 11 and 22 January 1993. For this purpose Dr. Kuschner brought a greater amount of vaccine and materials for preparing the solution in which the vaccine will be diluted.

At the end of the same month a quarterly working proposal for 1993 was sent to Dr. Jeanette Vega and Eduardo Araya, in accordance with what was requested by them, so as to define the remittance of resources to our Laboratory during this year (Appendix 4).

## Finance

The year 1992 finished with an outstanding debt of CH\$ 645,289 with the Iquique Health Service. A majority of it was the result of the last stage of the anti-cholera vaccination carried out in August 1992.

We had no obstacles in obtaining resources and paying bills by the Health Services in Iquique. The abovementioned debt was totally paid off by the PAHO during the first week of 1993 (Appendix 2).

An inventory of our Laboratory is enclosed herewith, updated to January 1993. (Appendix 3)

Yours faithfully,

Marcela Martínez Marco  
Meningococcal Project Nurse

Ricardo Bustamante Risco  
Project Supervisor

With Copy to:

Dr. Luis Martínez / Ministry of Health  
Dr. Jorge Toro A. / Ministry of Health  
Dr. Ramses Aguirre M. / Health Services Iquique  
Dr. Gustavo A. Mora / PAHO/WHO in Chile  
Dr. Antonio Marino M. / Regional Health Services 1<sup>st</sup> Region  
Dr. Patricia Gassibe / Ministry of Health  
Dr. Jeanette Vega / PAHO/WHO in Chile  
Dr. Lorian Castillo / Public Health Institute  
Mrs. Marcela Martínez / Project  
Dr. Ricardo Bustamante / Project  
File

\*\*\*\*\*  
\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
\*\*\*\*\*

Laboratory for Research  
into Meningococcal Disease

REPORT FOR JANUARY - APRIL 1993

Epidemiological surveillance

During this period we have recorded 12 cases of meningitis whose etiological distribution is as follows:

MENINGOCOCCUS	7
TUBERCULOSIS	1
VIRAL	1
Highly Suspect	1
Suspect	2

The highly suspect case corresponds to a child of 14 years of age in whom we only found some isolated gram (-) diplococcus in the gram tinction of gram, the results of the cultures of CSF and blood being negative.

The two suspected cases had altered CSF but not clearly indicative of a bacterial process, and it was impossible to isolate a germ in the samples analyzed.

The TBC meningitis corresponds to a secondary dissemination of a miliary TBC in an elderly woman coming from a rural semi-Altiplano community.

Of the 7 cases with a confirmed meningococcal etiology, 3 died because of meningococemia with hardly any meningeal invasion and with a sudden evolution in two of them. The evolution in the rest of the cases was optimal and they were all discharged in good condition with normal neurological and otorhinolaryngological (auditive) controls after discharge.

The case defined as highly suspect and one of the suspected cases were admitted into a private clinic in the city, which forced us to widen our coverage of surveillance to this sector. Furthermore, the collection methods and the processing of samples of CSF and blood obtained from these patients were reviewed with nurses and medical laboratory technicians of this clinic, not finding any differences with respect to those carried out in our

Laboratory which might explain the absence of the development of germs in the cultures analyzed.

The meningococcal disease rate in this first four-month period for Iquique is 4.18 cases / 100,000 inhabitants, with a mortality rate of 42.8%.

The monthly distribution compared to the last three years is:

	1993	1992	1991	1990
JANUARY	1	2	2	1
FEBRUARY	1	4	4	2
MARCH	2	2	2	4
APRIL	3	2	0	0
TOTAL CASES	7	10	8	5

The frequency according to sex has been greater in females during this period with a ratio of 2.5:1. Mortality was greater in men (100%).

Distribution by age and its comparison with the same period over the past three years is shown in the following table:

MENINGOCOCCAL INFECTIONS  
January - April (1990-1993)

No. of cases

Age range

This graph shows that there is a displacement of the disease over the past two years towards the younger age groups. The possible reason for this may be the greater immunological immaturity of this group added to the zero or low contact with the meningococcus which has not allowed them to build up immunological barriers against it, as in the case of adolescents and adults.

Among the cases recorded and bacteriologically confirmed we have found some in which there is a blood relationship and in which, because of the background information and the distance between one case and the next, cannot be called a secondary case. However, there is an hypothesis that in those family groups there might exist some immunological deficiency which is genetically determined. The corresponding authorities of the local Health Service were informed about this possible work area, but there is no definite plan as yet for evaluating this aspect.

## Educational Activities

Because of the appearance of several cases in a short period of time which caused three deaths, we held meetings with the pediatriatians and medical personnel of the Emergency Service of the Iquique Hospital at the end of March. Dr. Bustamante presented the current situation of the meningococcal disease in Iquique and its evolution since 1990. Some of the comments are included in the surveillance section.

At the same time, our Laboratory has prepared an educational program initially aimed at health care personnel working in the different peripheral outpatient clinics in order to explain the situation of meningococcal meningitis in Iquique and the way they can cooperate both in active surveillance and in the information and education to the community.

Mrs. Marcela Martínez has held meetings with the nurses of the outpatient clinics as well as those working in the private health care centers to review the field work that they have been carrying out with the contacts of ill patients, evaluating the field work and providing support in anything required (materials, receiving samples, taking pharyngeal smears, etc.).

Audivisual aids for education were prepared which included 22 slides explaining the meningococcal meningitis, its symptoms, steps to be taken and preventive measures. This was geared toward the community in general, and is complemented by a talk of a qualified member of the health team. This material is available for use by the Health Service.

On the occasion of the deaths occurred in March and April, interviews to Dr. Bustamante were published in the local press in which in addition to explaining the present situation, educational information is provided to the readers (see appendices).

A document was sent to the Health Authorities in Iquique requesting strengthening and updating all health care entities in Iquique regarding epidemiological surveillance norms and handling of contacts.

It was suggested to form a local meningococcal meningitis committee in which our Laboratory can participate as advisor to define guidelines, propose areas for research and provide information to the community, all from a single source.

Up to now our efforts have been supported by entities inside the Health Service which have other priorities and, therefore, have not given all the attention this issue requires.

In April, Dr. Bustamante went to a meeting convened by Dr. Toro at the Ministry of Health and in which Dr. Concepción Campa and Lourdes Almeida from the Research Center for the Production of Vaccines and Serum of the Carlos Finlay Institute from Cuba gave a presentation on an anti-meningococcal B vaccine and their experiences in Cuba and Brazil.

### RESPIRATORY ISOLATION

VISITORS : PLEASE REPORT TO THE NURSES' STATION BEFORE ENTERING THE ROOM

- 1- All persons approaching the patient must wear mouth covers.
- 2- A laboratory coat is not necessary
- 3- Gloves are not needed
- 4- WASH HANDS AFTER TOUCHING THE PATIENT OR ANY ARTICLE WHICH MIGHT BE CONTAMINATED AND BEFORE CONTINUING TO THE NEXT PATIENT.
- 5- All contaminated articles with any infectious materials must be disposed of or placed inside bags and labeled before being sent for disinfecting and reprocessing.
- 6- DISEASES WHICH REQUIRE RESPIRATORY ISOLATION.  
MENINGOCOCCAL INFECTIONS  
PAROTIDITIS  
PNEUMONIAS DUE TO HAEMOPHILUS INFLUENZAE  
MEASLES  
INFECTIOUS ERYTHEMA  
WHOOPING COUGH

In general, a private room is recommended for respiratory isolation; however, patients infected with the same germ may share rooms.

## CHEMOPROPHYLAXIS INSTRUCTIONS FOR MENINGOCOCCAL MENINGITIS

October 1992

- The chemoprophylaxis will be carried out with Rifampin for children under 16 years of age and Ciprofloxacin for those 16 years or older.

1- Children between the ages of 1 and 6 months will receive Rifampin Syrup 10 mg/kg/weight/day divided into two daily doses and they will be administered over two days.

2- Children of 6 months old up to 4 years and 11 months will receive Rifampin syrup (20 mg per Kg. per day) split into two doses over two days.

3- Children 5 years old up to 9 years and 11 months will receive Rifampin capsules (450 mg/day) divided into two doses over two days. Note: Rifampin comes in capsules of 150 mg.: Use 3 capsules daily.

4- Children from 10 years of age up to 15 years and 11 months will receive Rifampin capsules (600 mg/day) divided into two doses over two days. Note: The Rifampin comes in capsules of 150 mg.: Use 4 capsules daily.

5- Persons over the age of 16 will receive Ciprofloxacin 500 mg. in one dose.

Note: The Ciprofloxacin comes in capsules of 250-500-750 mg. The capsules which the service has at this moment are 500 mg. In any case, the dosage must be observed at all times.

If there are any reasons for not taking Ciprofloxacin, to the contrary, such as allergy to this drug, then Rifampin will be used.

### Rifampin:

Toxicity with brief treatment:

According to the literature, the highest frequency in adverse reactions with the use of this drug is 18.6% and the symptoms are slight.

Patients who receive treatment may suffer from head ache, sleepiness, sickness or gastrointestinal symptoms such as epigastric irritation, nausea, vomiting or diarrhea, all with a low frequency.

Rifampin may accelerate metabolism of oral contraceptives, this point only being important in those women who do not take them on a regular basis.

Ciprofloxacin:

The Ciprofloxacin has an incidence of adverse effects lower than 10% and which generally correspond to gastrointestinal irritation symptoms.

Exclusions from treatment for both antibiotics

- Persons with a history of allergies to Rifampin or Ciprofloxacin.
- Children 1 month old or less
- Pregnant women:
- History of Hepatitis:
- History of Alcoholism:

TABLE OF MEASURES FOR RIFAMPIN

1 month old up to 4 years and 11 months old (syrup)

1. Shake before using

2. The measure (lid) is marked with 2.5 cc - 5 cc - 10 cc.

3. The measure for 10 cc = 200 mg. Rifampin

The measure for 5 cc = 100 mg. Rifampin

The measure for 2.5 cc = 50 mg. Rifampin

5 kg - 6 kg = 5 cc daily (2.5 cc every 12 hours over 2 days)

7 kg - 8 kg = 8 cc daily (3.5 cc every 12 hours over 2 days)

9 kg - 11 kg = 10 cc daily (5 cc every 12 hours over 2 days)

12 kg - 14 kg = 13cc daily (6.5 cc every 12 hours over 2 days)

15 kg - 18 kg = 16cc daily (8 cc every 12 hours over 2 days)

19 kg - 22 kg = 20cc daily (10 cc every 12 hours over 2 days)

Greater weights will receive one dose per day over 2 days.

22 kg - 26 kg = 24 cc daily

26 kg - 30 kg = 28 cc daily

Between 18 and 25 kgs. If the child can take capsules of Rifampin, it will receive 450 mg. per day over 2 days. That means 3 capsules daily.

Children over 25 kgs. weight will receive 600 mg. per day over two days. That means 4 capsules daily or 30 cc of syrup.

MENINGOCOCCAL MENINGITIS  
IQUIQUE 1979 - 1992

Cases

years

MENINGITIS LABORATORY IQUIQUE

Meningococcal Infections 1991 - 1992  
Iquique Health Service

Meningococcal meningitis	Meningococc.	Deaths
--------------------------	--------------	--------

Aseptic meningitis	Purulent mening.
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Meningitis Laboratory

MENINGITIS 1992  
Bacterial Etiology

Cases

Meningococcus

Heamophilus infl.

Pneumoniae strept.

Etiology

Meningitis Laboratory

## INSTRUCTIONS FOR PARENTS REQUIRING INFORMATION FROM THE EMERGENCY SERVICE

Meningococcal disease (meningitis and meningococcemias) is serious and has been more prevalent in Iquique than anywhere else in the country for the past 10 years. In Iquique, the germ (meningococcus) that causes the disease is of the B type against which there is still no vaccine.

The disease can appear in persons of either sex and at any age, but is more widespread among children under 6 years of age.

In the Emergency Ward, the pediatrician examines your child for a moment and it is possible that the disease, if still in its initial stage, may not be apparent or under the guise of another illness and so the child is sent home.

### WHAT CAN PARENTS DO ?

Cooperate with the doctor, watch the child closely during 3 to 4 hours after being sent home, because the possibility exists that the meningococcal disease is only just beginning.

### WHAT SHOULD PARENTS LOOK OUT FOR ?

- Continuous fever (which does not respond to medicines)
- An intense headache
- Constant nausea, vomiting or diarrhea (which do not respond to medicine)
- Permanent weakness which affects the patient's relationship with others.
- When the child is very small, observe the following:
- If the child is UNCOMFORTABLE-CRYING-RESTLESS or if he/she is WEAK-INACTIVE and SLEEPS ALL DAY.
- If small spots appear upon the skin.

If the parents notice that the child does not respond to treatment given during those 3 to 4 hours of observation, they should immediately return to Emergency, and if possible consult the same doctor who saw the child before, giving him the results of their observation.

THIS OBSERVATION SHOULD BE SPECIALLY STRICT DURING THE NIGHT, BECAUSE SLEEP - OF EITHER THE CHILD OR ITS PARENTS - COULD PREVENT THE PARENTS FROM NOTICING ANY DECLINE.

EMERGENCY SERVICE  
IQUIQUE REGIONAL HOSPITAL

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\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
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Laboratory for Research  
into Meningococcal Disease

SCHEDULED ACTIVITIES 1993  
MENINGITIS LABORATORY

We are still working with the same staff as in 1992, who work the same number of hours. This is broken down as follows:

Supervising Doctor	4 hours daily	(1/2 day)
Nurse	4 hours daily	(1/2 day)
Auxiliary/Secretary	4 hours daily	(1/2 day)
Medical laboratory technician	2 hours daily	

The work done by each of the staff members has already been set out in detail in previous schedules and corresponds to obligations assigned in the latest contracts drawn up for the Period September to December 1992.

The salaries of the secretary and medical laboratory technician need to be raised in accordance with the CPI, plus a small incentive. If this happens, then their salaries will be as follows:

Secretary ..... \$ 70,000 monthly  
Medical laboratory technician ..... \$ 62,000 monthly

The salaries of the doctor and nurse would remain the same in US dollars, converted into their equivalents in pesos for payment.

A C T I V I T I E S

In the hopes that a new vaccine against group B meningococcus will appear shortly in Iquique and in Antofagasta, the epidemiological surveillance of all cases that appeared this year remains unaltered, and is as follows:

- 1) Recording all in-patients in the regional hospital or private clinics who are suspected of carrying meningococcal meningitis.
- 2) Keeping a file regularly updated of all cases of meningococcal infection based on the record sheet of clinical cases. Data

referring to meningitis of other etiologies and those which were not confirmed bacteriologically are also filed.

3) Supervising the work of obtaining, processing and evaluating the Laboratory examinations indicated for each patient and the cultures of pharyngeal smears taken from the contacts of these patients.

4) Home calls to all confirmed or suspected cases of meningococcal meningitis for obtaining epidemiological information as well as samples of serum of convalescent patients 21 days after the disease surfaces.

5) Tabulating all filed data in the case of meningococcal infection from 1987 up to this date, so that an exhaustive epidemiological, clinical and laboratory analysis in relation to the local situation over the past five years can be carried out.

6) Submitting these results to the principal Supervisor of the project for their review and authorization for publishing them.

7) Tabulating the results of the cultures of pharyngeal smears taken from contacts of patients with meningococcal infection, and comparing them with the results of similar previous experiences.

8) Organizing an educational program for health and other types of professionals and also the public in general in relation to meningococcal meningitis and probable angles from which this disease could be controlled in the future.

9) Administering an anti-cholera vaccine to those volunteers who initially received the placebo dose.

Dividing these activities in four-monthly periods, they would be broken down as follows:

A. January through April 1993:

Activities under numbers 1 through 4 were done. At the end of the period, a general report will be sent regarding the activities themselves.

The file data as set out in number 5 will be tabulated.

Planning the educational program as explained in activity 6.

Activity number 9 will be done in January 1993.

B. May through August 1993:

Activities 1 through 4 are kept without and changes. The activity report was sent to the principal Supervisor.

An analysis of the tabulation of data for activity 5 and its later submission for review and authorization for publication by the principal Supervisor of the project.

Tabulating results of activity 7.

Implementing the educational campaign in several areas in accordance with activity 8. This activity will be done with the help of physicians and other professionals from the local Health Service, but requiring a small financial contribution for stationery and audio-visual material for its completion.

C. September through December 1993

Activities 1 through 4 remain unaltered. A report was submitted regarding all activities up to the end of the period.

Analysis and submission of the results according to what was stipulated in activity 7.

The educational campaign of activity 8 continues with the help of the local media.

All these activities are contained within the normal working hours of the personnel from our Laboratory and sometimes overtime is necessary. There will not be greater expenses for overheads, and they will chiefly consist of stationery and some audio-visual equipment. Although not planned, the epidemiological surveillance team might travel to Antofagasta for assisting the start up of their activities..

Yours faithfully,

Dr. Ricardo Bustamante Risco

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\* MINISTRY OF HEALTH \*  
\* IQUIQUE HEALTH SERVICE \*  
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Laboratory for Research  
into Meningitis - Cholera

## GUIDELINES FOR HANDLING CONTACTS WITH MENINGOCOCCAL DISEASE

Pharyngeal meningococcal carriers are important in the appearance of meningococcal disease. There is evidence of a close relationship between the existence of carriers in one given community and the beginning, growth and decline of an epidemic. The carrier may be chronic, intermittent or provisional. If events exist which increase the presence of bacteria in the pharynx (for example: streptococcic pharyngitis), the number of pharyngeal meningococcus decreases at the same rate.

Even so, mere exposure to meningococcus, without which there is no disease, is not sufficient for its occurrence, and its appearance is linked to individual factors in the person exposed.

For the prevention of an outbreak of new cases in relation to one index case, it is essential to carefully observe all contacts with family, school mates and those in a same group in a day-care center; they must all be given immediate medical assistance if they become feverish.

The rapid use of chemoprophylaxis (within 24 hours of suspecting the diagnosis) is the best prevention we know against the appearance of new cases of meningococcal disease caused by sero-group B meningococcus. However, this alternative is not feasible because its mass application is very difficult, therefore, it must be restricted to risk groups made up of contacts consisting of family, contacts in day-care centers, kindergartens, children's homes and regiments. Habitual prophylaxis is not recommended for hospital staff or school mates and in the case of the former only if there has been intimate contact such as mouth-to-mouth resuscitation, intubation or aspiration of secretions from the patient).

The drug of choice for chemoprophylaxis is RIFAMPIN, which has demonstrated adequate efficacy which is maintained during 6 to 10 weeks. The use of Rifampin, however, may build up a resistance in 10% to 30% of all cases. This situation has not been studied at a local level, although from what has been seen up to now, no resistance appears to have been built up yet.

## GUIDELINES FOR HANDLING THE CONTACTS OF MENINGOCOCCAL DISEASE

From the moment the patient is admitted to hospital with a suspected or confirmed Meningitis, the following must be done:

1 - The doctor must immediately notify the Persons' Program Department by phone while the examinations confirm the diagnosis. This notification must also be done in writing on form RMC 14.

2 - Once the information has been received and within 12 hours, the nurse of the outpatient clinic nearest to the home of the patient should make an epidemiological home call on all contacts. For those cases of meningococcal meningitis, a contact is a person who:

- a. Sleeps under the same roof either permanently or sporadically.
- b. Has been living in the home of the patient at least one week previously although may not be there at this moment.
- c. Has maintained direct contact with the patient in another house, or the patient has made regular visits for one reason or the other.

The term "family" must be widened to include any family members who maintain close and permanent contact with the patient.

3 - In case the patient is breast-feeding or a pre-schooler who attends a day-care center or kindergarten, contacts are those youngsters in the same class or level of the sick child.

4 - If the patient is a person coming from an orphanage, children's home, regiment or prison, contacts will be determined according to the type of relationship maintained with the patient.

Contacts are not hospital staff, except those who have had intimate contact with the patient; accordingly for workers in factories, firms, offices, etc.

For school children, university or institute students, contacts are those who have maintained direct relationships with the patient in the two weeks prior to diagnosis of the disease.

Once the contact has been defined, the nurse will follow the instructions set out hereafter for handling contacts:

1. Take two nasopharyngeal smears at the same time from each of the contacts, completing all the contact's personal details, immediately sending the samples to the 5<sup>th</sup> Floor of the Laboratory. Do not forget that the culturette possesses a container for transporting the sample, and to release it, the ampoule that is found at its base must be broken.

2. After the nasopharyngeal sample has been taken, chemoprophylaxis (as indicated in the treatment instructions) must be administered immediately. It is very important to check that the treatment has been properly followed.

3. All those persons whose results of the pharyngeal smear are positive to *Neisseria meningitidis*, must have a new double pharyngeal control smear taken as soon as the result is known.

4. In the case of class, work or dormitory mates, a double nasopharyngeal smear must be taken in the first place, and those who are positive to *Neisseria meningitidis* must receive prophylactic treatment as well as a control smear.

NOTE: It is also important to follow up all family members OF THOSE WHO SHOW A POSITIVE SMEAR.

This means going to the positive contact's home and taking a double smear from them. Should any of them show positive, the same procedure as explained in point 4 will be followed.

The Persons' Program Department will contact the Laboratory to find out the results of the smear, duly notifying the corresponding outpatient clinics.

IQUIQUE HEALTH SERVICE  
MENINGITIS LABORATORY

IQUIQUE, 28 APRIL 1992

FROM : Dr. Ricardo Bustamante Risco  
Medical Project Coordinator

TO : Dr. Ramses Aguirre Montoya  
Director Health Service Iquique

Dear Doctor,

Owing to an increase in new cases of meningococcal meningitis and meningococemia which have broken out this year in the city of Iquique when compared to 1991, the Meningococcal Meningitis Surveillance Team hereby requests your permission to allow us to establish rules for home calls on all cases of Meningitis.

During such calls, the nurse will take a Pharyngeal Smear before administering chemoprophylaxis to each of the contacts.

The sample should be sent immediately to the Laboratory on the 5<sup>th</sup> Floor between 8 A.M. and 6 P.M. from Monday through Friday and between 8 A.M. and 12 noon on Saturdays, Sundays and holidays.

Dr. Fermín Mendez (Medical Laboratory Technician) will be responsible for these examinations in the Laboratory.

Thanking you kindly in anticipation, we remain,

Yours faithfully,

Marcela Martínez Marco  
Project Nurse

Dr. Ricardo Bustamante R.  
Project Coordinator

Copies to:

Dr. Jorge Santos DDPP  
Miss. Graciela Araya DAP  
File

MINISTRY OF HEALTH CHILE  
IQUIQUE HEALTH SERVICE  
MENINGITIS LABORATORY

IQUIQUE 28 APRIL 1992

Dr. Oscar González Valdés  
Medical Director (assistant)  
Regional Hospital  
Iquique  
by Hand

Dear Doctor,

Following our conversation yesterday regarding giving a talk on "Getting up to date on Meningococcal Meningitis" to the doctors, nurses and midwives of the Hospital, we are sending you a letter which is to be sent to the Services.

Thanking you for your kindness, I remain,

Yours faithfully,

Dr. Ricardo Bustamante Risco  
Medical Project Coordinator

MINISTRY OF HEALTH CHILE  
IQUIQUE HEALTH SERVICE  
MENINGITIS LABORATORY

IQUIQUE 28 APRIL 1992

FROM : Dr. Oscar González Valdés  
Director (assistant) Regional Hospital

TO : Medical Heads of Clinical Services

Owing to the fact that this year there has been an increase in new cases of meningococcal meningitis and meningococemia in Iquique when compared with 1991, the Meningococcal Meningitis Surveillance Team, within its action plan, will give a talk on "Getting up to date on Meningococcal Meningitis".

This may take place at the beginning of the clinical meetings, and for this reason we kindly request you, as Head of the Service, to send to my office possible dates of meetings so as to coordinate them all.

I would appreciate your extending the invitation to the nurses and midwives of the corresponding Services.

Thanking you kindly, I remain,

Yours faithfully,

Dr. Oscar González Valdés  
Director (assistant) of Hospital  
Iquique

MINISTRY OF HEALTH CHILE  
IQUIQUE HEALTH SERVICE  
MENINGITIS LABORATORY

Iquique, 1 October 1992

Dr. ....  
By Hand

The Laboratory researching Meningococcal Meningitis kindly invites you to a panel on "Getting up to date on bacterial meningitis : Etiopathogeny, handling, prevention, complications, local experience and a discussion" which will take place on Friday 9 October at 3 P.M. in the meeting rooms of the Chucumata Hotel.

Taking part will be: Drs. Elba Wu, head of the Infectious Diseases Unit of the "San Juan de Diós" Hospital; Carlos Acevedo S., infantile neurologist and professor in the Faculty of Medicine (West) at the University of Chile; Hector Olguin, Pediatrician and Immunologist, Head of the Blood Bank at the "Luis Calvo MacKenna" Hospital and Ricardo Bustamante, Meningitis Project Coordinator at the "Ernesto Torres Galdames" Hospital in Iquique.

Yours faithfully,

Dr. Ricardo Bustamante Risco  
Meningitis Project Coordinator  
Iquique

Dr. Ramses Aguirre Montoya  
Director of Health Services  
Iquique

MINISTRY OF HEALTH CHILE  
IQUIQUE HEALTH SERVICE  
MENINGITIS LABORATORY

IQUIQUE 28 APRIL 1992

FROM : Dr. Ricardo Bustamante Risco  
Medical Project Coordinator

TO : Juan Esteban Muñoz  
Director of Health Administration  
Municipal Corporation, Iquique

Dear Sir,

Owing to an increase in the number of new cases of meningococcal meningitis and meningococcemia that have broken out this year in the city of Iquique when compared to 1991, the Meningococcal Meningitis Surveillance Team would like to request your help in coordinating a talk on "GETTING UP TO DATE ON MENINGOCOCCAL MENINGITIS" for all doctors and nurses belonging to urban and well as rural outpatient clinics in Iquique.

This talk which is a part of the activities of the Surveillance Team may take place any day from Tuesday through Thursday and at times that do not hinder the proper running of the outpatient clinics.

We kindly request you to let this laboratory know an appropriate date.

Thanking you kindly in anticipation of your reply,

Yours faithfully,

Marcela Martínez Marco  
Project Nurse

Dr. Ricardo Bustamante Risco  
Project Coordinator

Copy to:  
File

## APPENDIX 1

Head of Research Laboratory:

### **Meningitis vaccine applied in Iquique did not work**

A total of 28 cases of meningitis, five of which resulted in death have been recorded so far this year in the city.

This was reported by Doctor Ricardo Bustamante, head of the Research Laboratory of Meningococcal Disease at the Regional Hospital. He added that the situation has puzzled the physicians.

He said the meningococcus produces inflammation and has a choice of settling in different parts of the body. Generally it settles in the meninges, which produces meningitis. "It can develop in the blood flow, which is called meningococcemia".

He said that from 1987 to date the mortality rate has been 7 percent. The figure is low compared to other countries, which reach 10 percent. "During that time there have been 146 cases, with an average of one or two deaths per year. In 1991, there were 21 cases and this year we have had 28, 5 of which have been lethal, all of the meningococcemia type, none from pure meningitis".

Doctor Ricardo Bustamante said this kind of disease unfortunately is not predictable, because it does not have controllable elements, and they are attributed to meningococcemia.

The last death from that type took place on Tuesday, October 27 and it affected a child two years and five months old. "The disease affects small children more. Their defensive system is not well formed, and according to statistics the most susceptible ones are between 6 months and 2 years of age".

He added there are several variables that are attributed to meningococcemia. "We do not know why meningococcus affects those cases and not others. Until now the origin has not been defined, no one knows where it starts and its transmission is viral".

## INCREASE

According to studies, the disease increases in the summer, because more people come to Iquique at that time of year for vacations and because of crowded conditions.

"Meningococccemia has a mortality rate of 40 to 50 percent this year, which is a higher figure than in previous years. This type of meningitis is in the study and research stage. It may be caused by a combination with type B meningitis".

- What was the result of the vaccine applied in 1991?

- It was not an effective vaccine, it only produced 51 percent. To have positive results, you need a minimum of 75 percent. But the group that brought the vaccine to Chile from the Walter Reed Hospital in the United States is still looking for a solution for this type of meningitis. It is committed to looking for a vaccine. Research has not stopped, and they are working on a new formula. They are in the study phase before bringing it to the city."

At the present time there is no vaccine available to apply in Iquique, but it could be ready at the end of 1993.

- Why did the disease increase this year, with a higher number of deaths, compared to previous years?

- The virus may have varied, perhaps, but with other characteristics. Also, we are continuing with tests of patients that have the virus, we are still continuing.

Unfortunately, because of the way it spreads, there are no protection methods for finding out its origin like cholera, for example. But the measures to take so the disease will not occur are avoiding crowded conditions, and that is almost impossible at the present time.

People who come in contact with a patient with the disease, the family or nursery school classmates, are given a pharyngeal smear test, which is a sample taken from the throat.

He added that since 1963 Iquique has been affected by a steady increase in cases of group B meningococcal meningitis. That led in 1987 to the implementation of a research laboratory of Meningococcal Disease which was in charge of applying a new vaccine to minors between one and 21 years of age.

At the end of 20 months of evaluation it was proven that it was safe with regard to the effects it could have on people, but not very effective in attacking the disease, and the possibility of mass vaccination was eliminated.

"Since 1987 the appearance of new cases of the disease declined gradually until 1991, and a close watch was kept on them through joint work carried out by the Health Service of Iquique and the Research Laboratory of Meningococcal Disease. He said

that this year there had been a moderate increase in the number of patients compared to the last few years. "Unfortunately because of the way it is transmitted through the air (drops of saliva from the patient), it is impossible to implement prevention measures that are really effective. The only option is to have a means of effective control through a vaccine, which is not available yet and is just in the initial stage of evaluation in the United States.

#### SURVEILLANCE

He said that the epidemiological surveillance that the Health Service of Iquique and the Meningitis Laboratory carry out consists of investigating the patient's contacts so that prevention measures can be applied to them in order to prevent the disease from spreading to other members of the family group.

## **MENINGOCOCCAL DISEASE IN IQUIQUE**

### Seasonal Variation



## **MENINGOCOCCAL DISEASE IN IQUIQUE**

### Distribution by Age 1987 - 1992

<u>Age Range</u>	<u>Percent</u>
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## **MENINGOCOCCAL MENINGITIS**

IQUIQUE 1979 - 1992

**Comment on interview**

Dear Director:

With regard to the publication in your newspaper on November 3, in which I am interviewed to find out about the current status of meningococcal disease in Iquique, I would like to make a few remarks. Expressions are used in the article that are not absolutely clear and, although they do not affect the purpose of the article adversely, they may confuse the reader.

I do not think it is necessary to repeat once again that the vaccine against meningitis from group B meningococcus was not useful, because this has been said on many previous occasions by various local health authorities since 1990, when the final results were obtained of the evaluation of the vaccine referred to.

The current situation of a moderate increase in the cases of meningococcal disease this year compared to last year, has caused concern in medical circles in our city rather than puzzlement, especially among the health authorities.

For that reason our Research Laboratory of Meningococcal Disease that has been working steadily since 1987 in close cooperation with the Health Service of Iquique, first on the evaluation of the vaccine and currently on active surveillance of all the cases of this disease that occur, has advised and supported the implementation of a number of measures for the best possible control of meningococcal meningitis. These measures are in full effect and they have been improved, with the participation of the local Health Service and the nurses who work in various outpatient clinics in the city. They consist of taking a nasopharyngeal smear (sample of secretion in the throat) from those people who are in direct contact with the patient with meningitis or meningococcemia and administering medicine to eradicate the possible presence of the germ in those people's throats.

The slightly higher frequency of the disease in the summer in Iquique is not significant, and the frequency of the appearance of cases remains more or less even during the year, unlike the experience in other countries where there is a clear predominance of this disease in the winter, because of the character of

transmission of the disease by air (drops of saliva) and more crowded conditions at that time of the year.

The reason for a higher number of patients with meningococcal meningitis this year is not at all clear. According to reports from the Institute of Public Health, the type of meningococcus the disease produces continues to have the same characteristics as in previous years. Therefore, it is not appropriate to suggest that there have been variations in the type of germ.

Meningococcal infection is produced by a bacteria, not a virus. This difference should be made clear, because since it is a bacterial infection there is antibiotic treatment for it, and in fact the reason that we have a low rate of deaths from the disease is because we have been able to provide adequate, early antibiotic treatment for patients. Unfortunately, because of situations attributable to the germ's increased aggressiveness, the patient's lower capacity of defense, or other factors that are not always well determined, the disease may have a fatal course despite all the medical support that is given the patient. That is what happens in meningococcemias, and until the present time neither here or anywhere else in the world have there been effective measures to avoid the serious course of this form of presentation of the disease.

The photograph included in the article is not realistic because the vaccine is applied in the arm intradermically, and it is applied with a gun especially designed for this purpose.

Thanking you for your newspaper's interest in reporting on a problem that is serious in our city and which the local health authorities are fully aware of. I think it is necessary to make these clarifications so that anyone who reads the article is not led to erroneous interpretations. I think the graphs that are included make it possible to have a more or less global idea of some aspects related to the meningococcal disease.

Thank you for your attention, and I hope there will be room for this letter in your newspaper.

Sincerely yours,

Dr. Ricardo Bustamante Risco, Supervisor of Meningitis Project.

**Because of accusation made by parents of child  
who died of meningitis**

**Investigation ordered of death in Hospital**

**IQUIQUE**

"We are going to start an investigation into the case of the child Priscilla Alvarez Rivas. We have to find out the details in depth, find out who took care of her, in what circumstances she reached the emergency room and, of course, talk to the professionals who took care of her. Only then are we going to have a clear idea whether we are going to carry out an investigation inside the hospital", said Doctor Eduardo Olguín, director of the Regional Hospital "Ernesto Torres" of Iquique.

The health professional made these statements when asked by **El Nortino** about the position of hospital management on the accusations made by relatives of the child Priscilla Alvarez Rivas, three years old, who accuse the personnel of the establishment of medical negligence.

"We can not take any kind of measure if we do not know the real situation. To carry out an investigation we have to have a general overview, which we do not have at this time", Olguín stated.

Despite insistent questions from the journalists, the director of the hospital did not give any more information about the names of the professionals who took care of the child, until they know, exactly, what took place from the first day the child reached the hospital until her subsequent death.

**ACCUSATION**

The Head of Pediatrics, Ricardo Bustamante, said "meningitis is very hard to diagnose because its symptoms are hard to define. Also, it is a very rapid disease, which can cause damage in a child in a few hours".

When asked about supposed medical negligence, he said that all the information is not in yet. "I also took care of the child, and I gave her an injection for fever and kept her under observation, which does not mean we were not concerned about the child. What happened is that Priscilla, at one moment, had a slight improvement which led one to think it was just a cold".

When **El Nortino** was asked about the relationship between the cousin who died last year of the same disease and Priscilla, he said that no common element has been detected up to the present.

"If the cousin had died a month ago, it would be reason to intensify the care, but in such a long period of time it is impossible for there to be any danger of contagion, which is what one might think of", Bustamante said.

Another point that upset Priscilla Alvarez's relatives a great deal was the fact that they were advised three days later that the child had suffered brain death.

On this subject the Head of Pediatrics said, "I think there was a misunderstanding; perhaps some of my colleagues did not know how to explain properly to the parents what the little girl had. But we tried until the last minute to save the child's life. The nervous system is very complex, and you can not say that brain death occurred at a specific moment".

Finally, the doctor recognized that it is very hard to give a very clear opinion of the circumstances that surrounded the little girl's death until they have all the necessary elements to make an analysis.

## **IQUIQUE**

### **Meningococcemia evolves suddenly**

Meningococcal infection, in other words, the infection produced by a bacteria called Neisseria Meningitidis or more commonly Meningococcus, generally has two main ways of manifesting itself.

The first is meningococcal meningitis, where the bacteria is almost exclusively located in the meninges which is a protective membrane that covers the whole brain.

And the second is meningococcemia where there is a massive passage of the bacteria into the blood flow, therefore into the whole organism.

The most frequent of the two forms is meningococcal meningitis and meningococcemia is the most serious one, although fortunately it is much less frequent, with a mortality rate that can reach 90 percent of the cases. This refers both to the local situation of this disease and also the way it appears in other countries and cities that are affected by it.

Besides these ways the infection appears, there is the so-called healthy pharyngeal carrier, who has the bacteria in his throat without having the disease.

This healthy carrier can be found in any population; he is found whether or not there is an outbreak of meningococcal infection.

The percentage of healthy pharyngeal carriers may fluctuate between two and five percent.

In our experience it has been approximately 1.2%.

Whether there are more or fewer healthy carriers is not related to the higher or lower frequency of meningococcal meningitis or meningococcemia.

In our city mortality from meningococcal meningitis has been zero, and the mortality has been exclusively attributable to meningococcemias. Fortunately the latter are only 17% of the meningococcal infections we have had in the last five years.

Unfortunately in most cases meningococcemia evolves suddenly, and it appears with very vague symptoms that would make it difficult to suspect the disease ahead of time, and even if it were diagnosed, it is very doubtful whether that could modify its fatal outcome.

Therefore, the recommendations of the Health Authorities are based on persistent observation of the patient in doubt.

### **Head of Meningitis Project:**

#### **"The disease affects very different countries"**

"If we compare the world situation we will realize that the problem of group B meningitis is not only in Iquique. It is in Cuba, Norway, it was in South Africa, and it is important in Brazil", Doctor Ricardo Bustamante, Head of Pediatrics and Physician In Charge of the Meningitis Project at the Regional Hospital said when asked about the probable impact of emissions from the fishing companies on the disease or climatic causes.

"It is hard to say superficially that it is a problem of the fishing companies. On the one hand, because this is a problem that affects several countries that are not very similar to our country. Climatically Cuba is much more tropical, Brazil, Sao Paulo also, but Norway is a strictly Nordic country, Scandinavian, and climatically it is not at all like ours. Moreover, they have a different kind of industry. Cuba, for example, does not have a fishing industry and it has a very high frequency of meningitis".

Asked about preventive measures assumed by the Service when a case is detected, he said that "treatment is given only and immediately to the nuclear family. In other words, to the direct contacts that are the people who live under the same roof with the sick patient. In other words, the children, father, mother, brother or grandmother. If there is a neighbor who the patient plays with in his house or in the neighbor's house, they are also given immediate treatment".

He emphasized that indirect contacts, in other words, classmates, playmates or residents of houses where the patient has had some contacts in the weeks previous to the illness are taken a pharyngeal smear test which is taking a sample from the throat to investigate whether they have the meningococcus. They are not given immediate treatment, but a pharyngeal smear is taken.

### **Outstanding participation of physician from Iquique**

A detailed presentation of the activity carried out by the physicians in Iquique, was made by Doctor Ricardo Bustamante, supervisor of the epidemiological surveillance program of meningococcal diseases in Iquique, on the Channel 12 program "Enfoque Regional".

The first program of the fourth season was moderated by journalist Ricardo Henríquez, who asked Doctor Bustamante about his participation in the work of the commissions of the Ministry of Health, which allowed him to explain the issue and also answer telephone calls made by the public.

The program is transmitted direct on Fridays, through the screens of Telenorte to the First and Second regions and questions can be made free of charge on the 800 line, number 550023, thus channelling the concerns of the television viewers, who receive an immediate response.

In 1990 the program won a prize from the National Television Council in the category of journalistic programs, and since then it has maintained an annual cycle with subjects of interest to the residents of the northern area.

Dr. Ricardo Bustamante:

**"No new cases of meningitis have been recorded"**

Since September of last year there have not been any new cases of meningococcal meningitis recorded.

Doctor Ricardo Bustamante, who is in charge of the Meningitis Program of the Health Service, reported this fact.

He said that in December of last year there were a few children hospitalized, who did not develop the infection in the end.

"We are in third place nationally in the number of cases, which indicates that obviously the patients have decreased. The great majority were discharged without any aftereffects, only one little girl died".

He assured that meningitis is a pathology, which has caused some alarm because of the way it spreads. "It is hard to imagine that people would not come to an outpatient clinic for help, because the symptoms involve the whole state of health of the patient affected. One of the problems is that there is not adequate control of the sale of medicine; there are relatives of the patient that give advice based on previous experience and exclude a professional check-up. Often this disease may look like a pharyngitis or diarrhea; afterwards the more obvious involvement of the meninges appears".

He indicated that there are symptoms that are classic, but even so the disease can not be diagnosed immediately. "There is always fever, vomiting, headache, among other symptoms".

He explained that one sign that was insisted on last year was observing the general state of the minors carefully, because bacterial meningitis produces a progressive decline when it appears.

When asked whether an increase in the rate of meningitis can be anticipated this year, he said it is hard to answer with certainty. "We think it may decrease, because in the previous period there were half the number of patients compared to 1992; that is the trend".

He emphasized that the problem with type B meningitis is that no vaccine has been found. "One has to keep up surveillance measures and be alert".

(graph)

## MENINGOCOCCAL MENINGITIS

IQUIQUE 1979-1993

Cases

years

### IQUIQUE MENINGITIS LABORATORY

The rate of meningitis has decreased compared to previous years.  
The statistics show that in 1994 these figures will remain steady.

## Project to eradicate carriers in Cariquima

### INTRODUCTION

From the months of July to October there were four cases of purulent meningitis from the area of Cariquima, an area in the foothills of the province of Iquique with a population of about 500 inhabitants. Three of these cases had a recognized meningococcal etiology (strain B:15:Pl.3), and for the rest it is possible to suspect it on the basis of the symptoms. The frequency is 800 cases/100,000 inhabitants/year, 30 times higher than the risk of contracting the disease in the city of Iquique, which is the city with the highest risk of contracting the disease in the country. The customary control measures were taken with family carriers, but there does not seem to have been any special contact among the cases, which leads one to suspect there is an increase in the rate of carriage of a meningococcus pathogen.

As the population is small and isolated, there was a possibility of trying to detain the outbreak by intervening the population en masse. The most feasible alternative is the eradication of pharyngeal carriers from the affected population. It should be borne in mind that this is a population that is mostly composed of Aymara indigenous people, which is dedicated to agriculture and cattle raising and has semi-nomadic patterns of life.

There are at least four similar experiments to the one proposed here that have been very successful: during epidemics from serogroup B meningococcus in 1976 and 1980 in an ethnically characteristic group in the Southwest of Alabama, U.S. (4,454 volunteers) and in an Eskimo community in Canada (844 inhabitants), respectively (1,2). Of the two, the latter is the most interesting one, because Rifampin was used and it reduced carriage in Eskimos from 32.4% to 0.8%.

The third experiment corresponds to one carried out in 1987 on a kibbutz population in Israel (3), with the B:4 serotype predominating. The rate of carriage of meningococcus was reduced from 7.1% to 0%, measured three weeks after treatment. In none of the studies mentioned did any new cases appear after the prophylaxis.

Unlike the previous ones, the study carried out in Iquique was a pilot experiment that did not intend to abort an outbreak. However, this experiment may be useful in indicating that two smears are necessary and sufficient to detect 95% of the carriers in a group, that the dot-blot technique based on the use of monoclonal antibodies is a quick tool for the detection of a specific strain, and that it is possible to reduce the level of

carriage significantly just by acting on carriers with chemoprophylaxis.

## MATERIAL AND METHODS

The whole population of Cariquima and surrounding villages (Quebe, Panevinto, Ancovinto, Ancuaque, Villablanca, Huaitane and Chijo) were included in the study.

Two pharyngeal smears were taken from each volunteer, according to the procedure used in previous experiments: taking the smear from the pharynx behind the uvula.

The methods of identification of the meningococcus were the same ones used in the pilot study and described in that protocol. The epidemic strain was determined, and the strains that had some of its characteristics. Afterwards, treatment was given to the inhabitants of the area, because there was information that the dot-blot method was not sensitive enough to detect all the carriers. That information was made public after the pharyngeal smears were taken.

Treatment consisted of giving Ciprofloxacin orally to adults in one dose of 750 mg., and Rifampin was given orally to minors under 16 in doses of 20 mg/kg/day, for two days with a maximum dose of 600 mg/day. Children under four years of age received two doses of 10 mg/kg for two days. Children under 6 months of age, pregnant women, people allergic to the drug, and people with a history of alcoholism or hepatitis were not given any treatment.

The health auxiliary was instructed to observe actively cases suspected of having the illness, referring them promptly, and notifying the local Health Service by radio. Active surveillance will be continued in the rest of the province.

## RESULTS

Double samples were taken from 382 inhabitants of Cariquima and the surrounding areas. 23/382 showed the presence of meningococcus with some characteristics of the epidemic strain and 8 of them were group B:15:P 1.3, which gives a rate of carriage of 2.09%, double the rate determined in the pilot study carried out in Iquique in 1990.

On a second visit to the place prophylactic treatment was given to 351/382 (91.8%) of the inhabitants studied previously. Seven pregnant women and 4 minors 6 months of age did not receive any treatment. Three pregnant women received treatment by mistake, and 3 adults were treated twice. Treatment was left for the remaining 31 people with the auxiliary at the local first-aid clinic.

Sixty-one people were treated without having a pharyngeal smear first. In summary, 401 people received antibiotics, 12 of whom did not belong to the locality. The latest census data on Cariquima obtained by the Municipality referred to 445 inhabitants, which results in an approximate coverage of chemoprophylaxis of 90.1%.

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PHASE 2 STUDY OF IMMUNOGENICITY OF THE WC/rBS ANTI-CHOLERA  
VACCINE IN A HEALTHY PEDIATRIC POPULATION IN IQUIQUE, CHILE

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The arrival of cholera in Latin America during 1991 inserted in the inadequate sanitary conditions that are found in many countries, indicates that this threat will remain in our country for many years before it can be resolved by significant investments in infrastructure in potable water, sewer systems with their respective treatment of sewage, and appropriate garbage disposal. A health structure with broad coverage and a higher level of sanitary education and hygienic behavior on the part of the population in those countries should be added to those control measures. Cholera is an endemic disease.

In our country, although it has been possible until now to control this contagious infectious disease, it is still necessary to improve several conditions like : treatment of sewage and its use in irrigation of fruit and vegetables that grow along the ground.

Meanwhile, besides maintaining the sanitary measures that the population has followed carefully, the health authorities are continuing to study the problem with concern because of its significant social and economic impact.

The Ministry of Health and some Health Services in the country and International Institutions are working on developing more efficient vaccines against this disease.

Experts from the PAHO/WHO recommended that they should start studying both the oral vaccine with whole dead cells/subunit B and the oral vaccine with live attenuated cells in several Latin American countries, and that if the results were promising, field testing should be held on a large scale in 1992-1993.

Therefore, it was decided to carry out phase 2 of this test in Iquique in conjunction with the Research Team from Walter Reed Hospital in Washington and the Team from the Research Laboratory on Meningococcal Disease of Iquique with the support of the Ministry of Health of Chile, the Health Service of Iquique and the Hospital of Iquique.

This phase lasted for 7 months (January 20 to August 20, 1992), and the purpose was to study the Immunogenicity of the anti-cholera vaccine, in other words, to measure the capacity of this

vaccine to raise the defense level of the organism to cholera in a group of 400 children, who were healthy Chilean adolescents between 2 and 15 years of age.

The vaccine was oral and it was diluted in juice; it consisted of dead cholera cells (WC), and a non-toxic part of the cholera toxin (rBS). This vaccine also had the quality of protecting against certain types of Escherichia Coli.

The children were incorporated into the study on a voluntary basis, and they were given a medical check-up to make sure they really were healthy.

The vaccine was administered in two doses at different intervals, and a booster dose was given 6 months later.

On January 20 the first dose was administered to 400 volunteers, after a medical check-up and blood test.

They received the second dose on different dates according to the groups.

All the vaccinated children were followed up to observe any reactions.

This activity took place at the 3 outpatient clinics in Iquique and the outpatient clinic in Alto Hospicio.

On August 3 the revaccination or reinforcement dose was initiated for 400 volunteers following the same procedure as the first time, with a medical check-up, blood tests and follow-up.

This stage was concentrated in our Laboratory at the Regional Hospital and the Alto Hospicio outpatient clinic.

The blood samples were sent to Sweden, where the behavior of our children's antibodies was studied with relation to this vaccine.

The final results will probably be ready at the end of the year or the beginning of 1993. In any case, all of the volunteers will be informed by letter and the community in general will be informed by the usual mass media.

It is our wish, and that of the whole team, that there will be a good response to this study and that it will be possible to carry out a study of the vaccine's efficacy so it can be administered in all of the countries with high risk.

Finally, it is important to point out the participation in this study of local health professionals like : Doctors, Nurses, Nutritionists, Medical Technologists. Also, Paramedics, Health

Monitors, Students in the Technical Paramedical Nursing Course,  
the Red Cross of Iquique and drivers in the Iquique Health  
Service.

We express our appreciation to all of them.

Marcela Martínez Marco  
Nurse Meningitis/Cholera Laboratory

ADMINISTRATION OF ORAL ANTI-CHOLERA VACCINE TO PLACEBO  
GROUP "STUDY OF IMMUNOGENICITY AND SAFETY OF ANTI-CHOLERA VACCINE  
PHASE II"  
IQUIQUE JANUARY-AUGUST 1993

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From January 1992 to August of the same year, phase II of the study of the anti-cholera oral vaccine was carried out on a volunteer group of adolescent children in the city of Iquique, Chile.

In the consent form given to the parents of the volunteers they were informed that a placebo volunteer group was necessary for this project, and at the end of the study they would be able to receive the anti-cholera vaccine if they wanted to (annex 1).

In conversation with the project team it was agreed to administer the vaccine in January 1993 with two doses at a one-week interval and a booster dose 6 months later. There were no previous check-ups or subsequent follow-up of the vaccination.

The placebo group (R4) consisted of 103 volunteers, 32 of whom were from Alto Hospicio, 14 belonged to Cami (Health care center for mothers and children), and 57 were distributed throughout different sectors of the city of Iquique.

Eight girls 12 years of age or over had to be given a pregnancy test before being vaccinated.

Program planning

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- 1 - Writing and sending letter with information to placebo group (annex 2).
- 2 - Coordination meetings with Cami on Friday, December 18.  
Coordination meetings with health personnel in Alto Hospicio, Monday, December 21.

### Schedule

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The vaccine will be administered in the Laboratory of the project (Regional Hospital).

I dose                      January 11 to 15                      from 8:30 to 12:00

II dose                      January 18 to 22                      from 8:30 to 12:00

Reinforcement dose on August 2 to 6 from 8:30 to 12:00.

### Human Resources

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Project Physician	: Dr. Ricardo Bustamante
Project Nurse	: Mrs. Marcela Martinez
Laboratory Assistant	: Mrs. Blanca Chamber

### Material resources

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Vaccine	n/a
Pregnancy test	n/a
Disposable cups	n/a
Plastic bags	50
Paper towels	2
Photocopy paper, letter size	103
Envelopes	103
Sending letters by telex	
General office supplies	n/a

IN JULY AND AUGUST A NEW DOSE OF VACCINE WILL BE ADMINISTERED.

WE WILL LET YOU KNOW THE DATE AT THE APPROPRIATE TIME.

EVERYONE AGAINST CHOLERA

EVERYONE

AGAINST

CHOLERA:

MINISTRY OF HEALTH

Life is first

IQUIQUE HEALTH SERVICE

CHOLERA:

IT IS AN INTESTINAL INFECTION THAT PRODUCES INTENSE, VERY FREQUENT DIARRHEA, LEADING RAPIDLY TO DEHYDRATION IF ABUNDANT LIQUID IS NOT GIVEN TO THE PATIENT.

DELAY IN SEEKING MEDICAL ATTENTION MAY RESULT IN DEATH.

THE MAIN FORM OF CONTAGION IS DRINKING CONTAMINATED WATER, CONSUMING VEGETABLES WATERED WITH SEWER WATER, AND EATING RAW FISH AND SEAFOOD.

THEREFORE THE BEST WAY TO AVOID IT IS WITH MEASURES OF HYGIENE:

potable water                      cooked vegetables

cooked fish and seafood              covered garbage

BUT TO HELP AVOID THE APPEARANCE OF AN OUTBREAK OF CHOLERA EVEN MORE IT WOULD BE HELPFUL TO HAVE AN EFFECTIVE, SAFE VACCINE

THE MINISTRY OF HEALTH OF CHILE, THE PAN AMERICAN HEALTH ORGANIZATION AND THE IQUIQUE HEALTH SERVICE WANT TO TEST THE USEFULNESS OF A VACCINE AGAINST CHOLERA.

THIS VACCINE IS ORAL AND WE WILL USE IT ON A GROUP OF VOLUNTEER CHILDREN, BETWEEN 2 AND 15 YEARS OF AGE, WHO WILL RECEIVE 3 DOSES.

ON

JANUARY

**20**

WE WILL TAKE A BLOOD SAMPLE AND THEY WILL RECEIVE THE FIRST DOSE OF VACCINE.

YOUR CHILD WILL RECEIVE A SECOND DOSE OF THE VACCINE ON

AT \_\_\_\_\_  
AND WE WILL TAKE A NEW BLOOD SAMPLE ON

DON'T FORGET THAT YOUR CHILD SHOULD NOT RECEIVE ANY KIND OF FOOD  
(SOLID OR LIQUID) ONE HOUR AND A HALF BEFORE AND AFTER RECEIVING  
THE VACCINE.

**Let's work together**

**against Cholera**

- Voluntary vaccination  
against cholera.  
Children between 2 and  
15 years of age. (Oral)
- Vaccination:  
August 3, 1992 at  
Hospital. 6th floor.  
(Cholera-Meningitis  
Laboratory)
- If you are interested,  
come to the nearest  
outpatient clinic for  
more information, or  
call 426014.

**BOOSTER  
DOSE**

Everybody together against cholera

MINISTRY  
OF HEALTH

IQUIQUE HEALTH SERVICE

Ministry of Health arranged for 400 children and adolescents in  
Iquique

**THEY WILL APPLY VACCINE  
AGAINST CHOLERA**

On the 20th the massive vaccination program starts against cholera. Four hundred children and young people between 2 and 15 years of age will participate in the study.

The information was provided yesterday by Doctor Ricardo Bustamante Risco, coordinator of the health team of the "Dr. Ernesto Torres Galdames" Hospital, which pediatrician, Claudia Aburto, and registered nurse, Marcela Martinez, are also part of.

He reported that the hospital's research laboratory has a vaccine made in Sweden, provided by specialists at Walter Reed Hospital in the United States.

The objective of the program is to use the vaccine on children and young people, from 2 to 15 years of age, to find out how much protection it provides against the disease. It is known to be effective in the adult population and does not generate any side effects, but it has not been defined how long its protection lasts in the infantile population.

The study is going to be carried out on 400 children, on a voluntary basis. The parents only have to sign an acceptance letter similar to the system used for the vaccine against meningitis.

The vaccine will be administered orally, diluted in a bicarbonate solution (75 ml. for those younger than 5 and 150 ml. for those over 5), with each child receiving two separate doses at different intervals, according to the study group they are in; there will also be a control group of one hundred children who will receive just the bicarbonate solution.

In order to determine the capacity for producing antibodies against cholera in each child that receives the vaccine, blood samples will be taken at the beginning of the study, two weeks after the second dose of vaccine, and then two more samples will be taken with a two-week interval, six months after the beginning of the study.

The volunteers will be kept under close clinical supervision during the study. The researchers or nurses who collaborate on the project will interview and examine the minors at least once a day for three days after each dose of vaccine is administered.

## CALL

Doctor Ricardo Bustamante pointed out that up to now only 250 children have registered, and they need 150 minors to complete the number needed for the vaccine's application.

The physician called on the parents to register their children at the Cirujano Guzmán and Videla outpatient clinics. They can also call the telephone at the hospital laboratory: 426014.

The results will be announced in September and October, after the analysis and the result of the samples that will be done at the University of Goteburg, Sweden.

He reported that the country is not exempt of the disease, adding that studies have revealed that the germ is alive in the sewers and in the waters of the Azapa Valley.

He pointed out the presence of 13 new cases of cholera in Tacna and recently in Bolivia, converting the Tarapacá region into a high-risk area.

He explained that the appearance and maintenance of cholera is closely linked to a country's sanitary conditions (poor conditions of potable water, sewer system, sewage treatment, elimination of garbage).

He emphasized the labor done by the World Health Organization, which is investigating some vaccines against cholera, carrying out studies in Asian countries where it is applied to children under 10, without resulting in any side effects.

### **They will apply vaccine against cholera**

Specialists from the Ministry of Health of Chile and the United States will start an immunogenicity study of the vaccine against cholera next January.

The information was provided yesterday by Doctor Ramsés Aguirre, Director of the Health Service, who was accompanied by the American specialists, Robert Kuschner and Wendell Zollinger; doctors Jorge Toro, Head of Epidemiology and Patricia Gassibe, epidemiologist of the Ministry of Health, and Doctor Ricardo Bustamante and Nurse Marcela Martinez, of the Health Service.

The American team is not the same group of specialists who have been participating in the study of the vaccine against meningitis since 1987 that will conclude next year.

Four hundred children, whose parents volunteer to participate in the experiment, will be vaccinated. The study consists of measuring the capacity of the vaccine to raise the defense level of the organism against cholera, and as indicated, it has already been tested on groups of adults in the United States, without observing any side effects. There is also a study that included 63,000 individuals, which took place in Bangladesh, with another very similar vaccine, without any adverse effects being observed in that case either.

The specialists said that the arrival of cholera in Latin America in 1991, inserted in adverse sanitary conditions, indicates the threat will last for many years in the country, before problems like potable water, sewer systems with the respective treatment of sewage, and proper disposal of garbage can be resolved with important investments in infrastructure.

They also manifested that a health structure, broad coverage, and a high level of sanitary education and hygienic behavior among the population should be mentioned.

They added that although it has been possible to control contagious infectious disease in the country, several conditions have to be improved like treatment of sewage and its use in watering fresh vegetables that grow along the ground.

Doctor Ramsés Aguirre presented the team of specialists, composed of Chilean and American doctors, who will expedite a project of systematic vaccination that is going to be tested in the city, which has been described as a "virgin cholera area".

Doctor Jorge Toro, Head of Epidemiology of the Ministry of Health, explained that the vaccine has already been applied to 63,000 Swedish citizens, and 300,000 doses were applied to contingents that went to the Persian Gulf. He explained, however, that the specialists want to see the immunological response in children which is the reason the health team asked the parents of the children to volunteer if they want to take the test, so they can measure exactly the level of antibodies the vaccine can produce, in other words, what the adequate dose is against cholera.

The specialist insisted that this is a vaccine to protect children basically; he pointed out that a similar experiment is already being carried out in the northern part of Santiago.

Robert Kuschner, an American specialist, explained that the complete study is going to be finished in August, and the results will be analyzed in a Swedish laboratory. The final results of the experiment will be delivered in November of next year.

Doctor Ricardo Bustamante pointed out that the vaccination will be carried out in the second half of January. It consists basically of two doses of vaccine that will be applied in different amounts to the 400 children chosen, adding that it is an oral dose that is diluted in a bicarbonate solution.

The age of the children will vary between two and fifteen years, and they will be chosen after a letter of consent is signed by their parents in the presence of a witness.

The registrations are received in the medical laboratory of the Health Service, phone 426014. Call Doctor Ricardo Bustamante and Nurse Marcela Martínez.

### **Vaccination continues today against cholera in Alto Hospicio**

The vaccination program against cholera continues today in Alto Hospicio. It is coordinated by the Health Service and Walter Reed Military Hospital in the United States.

The program, which implied the massive vaccination of four hundred children between two and fifteen years of age, consisted of the oral administration of the vaccine, diluted in a bicarbonate solution in doses for children below five years of age and those over five.

Doctor Robert Kushner, a researcher from Walter Reed Hospital, expressed his apprehension about whether the community would respond to the call made by the health authorities to get the 400 children needed for the experiment.

The specialist, who administered the vaccine in plastic cups, with a salty cherry flavor, stayed in the Videla outpatient clinic all morning, supervising the application.

Marcela Martínez, registered nurse, informed the newspaper that the vaccination process was taking place normally in the three outpatient clinics designated by the Health Service.

This newspaper went to the Cirujano Videla outpatient clinic, located in the La Puntilla neighborhood, where it confirmed that the process was taking place normally, observing parents waiting for their children to receive the vaccine since early morning.

The personnel was in three rooms, perfectly equipped for the application of the vaccine. Doctor Francisco Espinoza, registered nurses Isabel Venegas, María Antonieta Vargas and Lucy Donaire, and the researcher from Walter Reed Military Hospital, Robert Kushner, participated.

Marcela Martínez, of the health team, said the vaccination process was carried out in three phases: a medical check-up to confirm the good state of the minor's health; the extraction of a blood sample and consumption of the vaccine.

According to the schedule, the 400 children should return to the outpatient clinics on January 27 for the second dose and on February 10 for the second blood test.

Later, between July and August of this year the third dose will be applied.

## OPINIONS

Marta Durán Muñoz, mother of the little girls Marisela and Carmen Altamirano, 13 and 5 years old, said that she decided to vaccinate her daughters to protect them from the disease. "We talked it over with my husband and we decided the children should be vaccinated".

Manuel Tapia, a nurse's aide from the Hogar del Niño, said that the invitation for the minors to be vaccinated came to the home in the form of an official document.

Then the parents signed the consent letter. The next children were vaccinated: Raúl Luna, 14 years; Marcos Rivero, 12 years; Manuel Alcota, 10 years; Juan Alcota, 7 years; Victor Daza, 7 years; Abraham Tapia, 8 years and Ulises Tapia, 9 years.

Regarding the vaccination, Manuel Tapia answered that "I think it is necessary, but I don't know whether it is positive. This is an experiment, and somebody has to do it. In any case it does not have any side effects". Mary, two years old, described the vaccination as positive.

## LETTER

The Health Service, in the consent letter sent to the parents, stated:

"Cholera is a contagious disease that is transmitted through water and food contaminated by a bacteria called vibrio cholera that leads to dehydration that can be fatal if it is not treated in time".

It added that "at the present time there is a vaccine that is given that is available in our country for use in school children in Iquique. This vaccine has already been used in Sweden and the United States without producing any kind of reaction.

"The children who participate should be healthy".

"A group of children will receive the vaccine and another group will receive another substance that is not a vaccine; that is to prove that the vaccine is really safe and produces protective immunity. Your child will be in one of the two groups, which will be formed at random".

MINISTRY OF HEALTH  
IQUIQUE HEALTH SERVICE

Research Laboratory  
Meningitis - Cholera

C E R T I F I C A T E

I certify that the contents of the cargo shipped to Dra. Ann-Mari Svennerholm, University of Goteburg, Sweden, corresponds to samples from the study of an anti-cholera vaccine carried out in the city of Iquique. This study is backed by the government of Chile through the Ministry of Health.

These samples do not constitute any danger of biological contamination to anyone who manipulates and transports them. They may be transported on regular commercial flights without any special precautions.

Dr. Ricardo Bustamante Risco  
Supervisor Meningitis-Cholera Project

Iquique, September 8, 1992.

MINISTRY OF HEALTH OF CHILE  
IQUIQUE HEALTH SERVICE  
MENINGITIS/CHOLERA LABORATORY

Iquique, August 31, 1992

Dr. Ramses Aguirre Montoya.  
Director Iquique Health Service  
City  
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Dear Doctor :

The Meningitis/cholera Commission would like to present its compliments and express its appreciation for your special cooperation with the anti-cholera vaccine study by giving facilities to the medical and paramedical professionals to participate on our teams and also facilitating vehicles and drivers to transfer personnel of the Project and the Service.

Both this study and the Meningitis project, as they are a different way of focussing the health problem, basically require the support of your Service, and we have to make contributions to help those programs to operate properly.

The analysis of the work carried out during these 7 months of study will be provided at meetings planned in conjunction with the Service, and the results will probably be ready at the end of the year or the beginning of next year.

We thank you once again for your help.

Sincerely yours,

Marcela Martínez Marco  
Project Nurse

Ricardo Bustamante Risco  
Project Supervisor

## Evaluation of anti-cholera vaccine phase II

On August 3 the last stage in the evaluation of an anti-cholera vaccine started on 485 volunteers between 2 and 15 years, who had been incorporated into this study between January and March of this year to carry out the initial stage. (Annexes 3 and 4).

At that time the volunteers were submitted to a blood test before the administration of an oral dose of vaccine (or placebo as applicable) and later to a last blood test 15 days after receiving the vaccine or placebo.

A total of 408 children finished the study. The samples collected from the minors will be sent to Sweden and the United States to determine the production of antibodies against vibriion and vibriocidal activity.

In this stage we had the cooperation of a number of nurses from the Health Service and Municipal nurses, as well as students from the nursing aide course who were a great help in carrying out this activity properly.

It is also necessary to point out the support provided by the Iquique Health Service in providing vehicles and drivers which were essential to transfer personnel to the different work sites.

Drs. Robert Kuschner, Andrew Trofa, Konrad Hayashi, and the medical technician Mr. Higinio Bustos travelled from the United States to work on this stage.

The final results of this study will probably be available at the end of the year, when the pertinent information will be given to the local health authorities and the volunteers who participated, with diffusion in the press.

The volunteers who received the placebo dosis were offered the oral anti-cholera vaccine in two doses at a two-week interval in the month of September.

MINISTRY OF HEALTH OF CHILE  
IQUIQUE HEALTH SERVICE  
MENINGITIS/CHOLERA LABORATORY

FROM : DR. RICARDO BUSTAMANTE

TO : MRS. GLADIS GOMEZ  
Accounting Dept.  
Iquique Health Service

Dear Mrs. Gladis :

As you know, this Laboratory has just finished the third and last stage of the anti-cholera vaccination of a group of 400 Chilean adolescents. To do this study a team of nurses and paramedical professionals was needed who had to receive the volunteers, take blood samples, give vaccinations, follow-up and transfer volunteers and teams to the different work sites. They should be paid the following:

Lucrecia Inostroza Chepillo	\$ 10,000
Julia Cam Aguirre	15,000
Edita Sanchez Garate	35,000
Monica Luna Cabezas	15,000
Smirna Pozo Godoy	15,000
Consuelo Riquelme Vitalis	15,000
Alfredo Rodriguez Ibañez	10,000
Elena Gonzalez Acevedo	40,000
Carla Hurtado Cam	15,000
Milagro Mancilla Varas	5,000
María Inés Vergara Castillo	10,000
Lidia Arellano Contreras	5,000
Ma. Antonieta Vargas Rodríguez	5,000
Carlina Leon Rivas	10,000
Juan Troncoso Santana	15,000
Jaqueline Marchant Crespo	7,500
Lucy Donaire Caceres	10,000
Pedro Arriaran Miranda	10,000
Mauricio Law Benavides	10,000
Arturo Burgos Fuentes	2,500
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Total	\$ 260,000

Sincerely yours,

Mrs. Marcela Martínez Marco  
Project Nurse

Dr. Ricardo Bustamante  
Project Coordinator

WORK TEAM 1992

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A 10-liter gasoline voucher is added to this for follow-up

Blood Sample	:	\$ 10,000 whole day
Reception	:	\$ 5,000 whole day
Vaccination	:	\$ 5,000 whole day
Follow-up for two days	:	\$ 10,000
Transportation of team	:	\$ 10,000 whole day
Additional help	:	\$ 5,000 whole day

Lucrecia Inostroza (Nutritionist)	:	August 3 - Reception 1
		August 4 - Vaccination 1

Julia Cam (Nurse)	:	August 3 - Reception 1
		August 4 and 5 - Follow-up

Edita Sánchez (Nurse)	:	August 3 - Samples 1
		August 4 and 5 - Follow-up
		August 17 - Sample 1/2
		August 18 - Sample 1/2
		August 19 - Sample 1/2

Monica Luna (Nurse)	:	August 3 - Sample 1/2
		August 4 - Sample 1/2
		August 17 - Sample 1/2

Smirna Pozo (Nurse)	:	August 3 - Sample 1/2
		August 17 - Sample 1/2
		August 18 - Sample 1/2

Consuelo Riquelme (Nurse)	:	August 3 - Sample 1/2
		August 4 - Sample 1/2
		August 18 - Sample 1/2

Alfredo Rodríguez (Nurse)	:	August 3 - Sample 1/2
		August 17 - Sample 1/2

Milagro Mancilla (Nurse)	:	August 4 - Sample 1/2
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Carlina León (Nurse)	:	August 4 - Sample 1/2
		August 18 - Sample 1/2

Elena Gonzalez (Nurse)	: August 4 - Sample 1
	August 5 - Sample 1
	August 18 - Sample 1
	August 19 - Sample 1
Ma. Inés Vergara (Nurse)	: August 4 - Follow-up
	August 5 - Follow-up
Lidia Arellano (Nurse)	: August 17 - Sample 1/2
Ma. Antonieta Vargas (Nurse)	: August 19 - Sample 1/2
Carla Hurtado (Nursing Intern)	: August 3 - Vaccination 1
	August 4 - Follow-up
	August 5 - Follow-up
Jaqueline Marchant (Nursing Aide)	: August 3 - Help Sample 1
	August 4 - Help Sample 1/2
Lucy Donaire (Nursing Aide)	: August 3 - Help Sample 1/2
	August 4 - Help Sample 1/2
	August 17 - Help Sample 1
Juan Troncoso (Medical technician)	: August 4 - Sample 1/2
	August 18 - Sample 1
Pedro Arriarán (Serv. Driver)	: August 3 - Transfer 1
	August 4 - Transfer 1
	August 18 - Transfer 1/2
	August 20 - Transfer 1/2
Mr. Mauricio Lau (Serv. Driver)	: August 17 - Transfer 1
	August 18 - Transfer 1
	August 19 - Transfer 1
Mr. Arturo Burgos (Serv. Driver)	: August 19 - Transfer 1/2

**Study of Carriage Neisseria Meningitidis in 872 pharyngeal smears of contacts of Patients with Meningococcal Meningitis. Iquique Hospital, May 1992-1993.**

**Dr. Ricardo Bustamante Risco  
Mrs. Marcela Martínez Marco, R.N.  
Research Laboratory of Meningococcal Diseases  
WRAIR - PAHO - MINSAL Project  
IQUIQUE**

**INTRODUCTION**

Pharyngeal Carriage of Neisseria meningitidis (meningococcus) is the most frequent form of presentation of diseases of the meninges without constituting a clinical entity in itself; its importance lies in the fact that it is the gateway to other clinical manifestations of this infection which are mainly meningitis and meningococcal sepsis (meningococcemia).

According to the description, no more than 1% of pharyngeal carriers develop any form of disease, and in any population the percentage of pharyngeal carriage of meningococci fluctuates between 1% and 5%, rising to between 5-10% when there is an epidemic.

The city of Iquique has presented an epidemic situation with relation to meningococcal disease since 1980 and the epidemic strain corresponds to Group B serotype 15 1.3. A vaccine was developed by Dr. Wendell Zollinger in WRAIR (U.S.), for which purpose an efficacy test was carried out in 1987 which showed an efficacy of -23% between 1-4 years and 69% between 5-21 years with global efficacy of 51% at 20 and 30 months of follow-up.

Although no direct correlation is described between the development of an epidemic because of meningococcal infection and

carriage of the meningococcus in the population affected, in light of the marked increase in cases of meningococcal infections with significant mortality in the first five months of 1992, which contrasted with a downward trend in the previous years (1989 Rate 23.5, 1990 rate 11.9), we wanted to evaluate this carriage among the contacts of those patients where the presence of meningeal infection was confirmed and also where there was meningitis without bacteriological confirmation of the germ. That way we intended to identify early a high presence of pharyngeal carriage of meningococcus that implied an increase in the risk of acquiring a meningococcal infection. Along with that we also wanted to evaluate the efficacy of Ciprofloxacin and Rifampin in the eradication of pharyngeal carriage of *Neisseria meningitidis*.

The incorporation of Ciprofloxacin was considered, to be administered in one dose to those over 15 years of age because there was little adhesion to prophylactic treatment with Rifampin in that group. This antibiotic was used in a pilot study in chemoprophylaxis of carriers of *Neisseria meningitidis* group B in March of 1990 in Iquique. This was done to measure the efficacy of treatment with Ciprofloxacin in the eradication of healthy pharyngeal carriers in the medium term, as well as the decrease in the general rates of carriage in the population being studied.

A similar experiment with this drug was made in a community in the Altiplano (highlands). In both studies there were excellent results.

## **OBJECTIVES:**

- Determine prevalence of pharyngeal carriage of *Neisseria meningitidis* and the group B epidemic strain in high-risk population for the period of one year (May 1992 - 1993).

- Verify the efficacy of Ciprofloxacin and Rifampin as chemotherapeutics for the eradication of pharyngeal carriage of *Neisseria meningitidis*.

- Establish comparison with similar studies of carriage carried out in Arica (1989 school-age group) and Iquique (meningococcal vaccination 1987 study group).

## **METHODOLOGY:**

According to the norms imparted by the **MINSAL** (Ministry of Health) and local guidelines used until the beginning of this study, all the contacts (who live under the same roof) of confirmed patients or those suspected of carrying a meningococcal infection were given chemoprophylaxis with Rifampin in two daily doses for four days.

In light of the appearance of two secondary cases at the beginning of 1992 that did not correspond to people who lived in the same place as the patient but had had some tangential contact with him in the days before the disease appeared, and therefore did not receive prophylactic treatment, it was decided to broaden the concept of contact including those people who had had frequent contact with the index case up to 10 days before his admission to the hospital.

A laboratory record book was opened for the study that included the contacts of confirmed patients or those suspected of carrying a meningococcal infection and those who asked for it spontaneously because of some connection with a patient hospitalized for that pathology.

On the basis of this record a data base was created with the Dbase III program that included:

- No. of study
- Full name
- Age

- Sex
- Residence
- Type of contact with patient
- Pharyngeal smear (dates)
- Results
- Treatment
- Control

Data analysis was done using the Epi-Info program.

All the contacts with positive results to Neisseria Meningitidis, without determination of serogroup, were treated with Rifampin for two days (under 16 years of age) and 500 mg. of Ciprofloxacin in one dose (16 years and over).

A double pharyngeal smear was done for control of positive contacts, and there was follow-up for a year of the whole group in the study.

The primary health care nurses were trained in the guidelines for handling contacts, including how to take a double pharyngeal smear, and the shipping of samples to our laboratory for processing and analysis was coordinated.

#### **BACTERIOLOGY:**

Two nasopharyngeal cultures were taken, obtaining a sample by scraping the rear pharyngeal wall immediately above the level of the soft palate with a curette.

The cultures were sown immediately in Thayer - Martin medium, and they were incubated after two hours at 37 degrees Celsius in a CO2 atmosphere. The organisms obtained from these cultures after 24 hours of incubation were identified as Neisseria meningitidis, if they were oxidase (+) and if they only fermented glucose and maltose later (Quad - Ferm).

These samples were sent later to the Public Health Institute which confirmed the germ and determined the serogroup and serotype.

**TABLE N° 1**

**PREVALENCE OF PHARYNGEAL CARRIAGE**  
**High-Risk Group Iquique. May 1992-1993**  
**N = 872**

AGE	SAMPLES	LACTAMICA	POSITIVE	NEGATIVE	OTHERS
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**TABLE N° 1-A**

**PREVALENCE OF EPIDEMIC STRAIN BY AGE GROUP**  
**High-risk Group Iquique. May 1992-1993**  
**N = 88**

AGE	SAMPLES	N. MENINGIT	B	B.15.1.3	OTHERS	GROUP. N°
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**TABLE N° 2**

**DISTRIBUTION PS SAMPLES ACCORDING TO SEX**  
**High-risk Group. Iquique May 1992-1993**

RESULTS	MASCULINE	FEMININE	TOTAL
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SAMPLES

NEGATIVES

LACTAMIC NEISSERIA

N. MENINGITIDIS

GROUP B N. MENINGITIDIS

**TABLE N° 3**

**DISTRIBUTION OF RESULTS OF PHARYNGEAL SMEARS  
According to Age Group.  
Comparative Chart 1987 and 1993 Studies**

IQUIQUE 1987

n = 1017

VACCINATED GROUP

IQUIQUE 1993

n = 529

RISK GROUP

AGE

**STUDY OF CARRIAGE IN ARICA (1989)**

**N = 2021**

**School-age Group**

AGE

NEGATIVE

LACTAMICA

N. MENINGIT

B 15 1.3

**TABLE N° 4**

**CHART OF PROPHYLACTIC TREATMENT, HIGH-RISK GROUP**

**June 1992 - June 1993**

**N = 88**

JUNE 1992                      48 - 72 HRS.                      JUNE 1993

Rifampin

Ciprofloxacin

UNTREATED

\_ One was treated again with Rifampin because it was not certain that adequate prophylaxis had been carried out, and the other one with Ciprofloxacin, and both had negative results in the control carried out 72 hrs. later.

**RESULTS:**

The prevalence of pharyngeal carriage of meningococcus in the risk population studied (872 contacts of patient hospitalized for meningeal infection with confirmation or suspicion of meningococcal etiology) was 10.0%, and it was 18.1% for Lactamic Neisseria.

Germ was not isolated in 68.2% (Table N° 1)

In cases where Neisseria meningitidis was isolated, 2.6% corresponded to group B, and 1.5% corresponded to the epidemic strain (B.15.1.3) (Table N° 1-A).

The highest frequency in carriage was observed in the 14 to 19 age group (19.3%), and the lowest frequency was in the 1 to 5 age group. A higher proportion of Lactamic Neisseria (38.2%) was found in the latter group.

When analyzing the prevalence of carriage according to sex, men are seen to have a higher frequency of carriage of *N. Meningitidis* (59.0%) than women (40.9%), and this difference becomes more marked when considering the epidemic strain, reaching almost twice as many cases in men (61.5% versus 38.4%) (Table N° 2).

It is interesting to observe the prevalence of carriage in a study group from 1 to 19 years of age (subgroup of vaccinated young people = 1017) in 1987 as, when compared with the same age range in our study, a marked increase is seen of Lactamic *N.* in the latter in all age groups. Compared to the carriage of *N. meningitidis* and the epidemic strain there is a slight decrease (1.9% to 1.3%) (Table N° 3).

Of the 872 contacts studied, *N. meningitidis* was isolated in 88 of them (10.0%). Forty-nine were treated with Rifampin, 33 with Ciprofloxacin and 6 refused treatment (Table N° 4). In the group treated with Rifampin we had a loss of 18% in the control carried out 48 - 72 hrs. post-treatment which remained the same in the control one year later, with a final efficacy of the chemoprophylaxis with Rifampin of 90.0%.

In the group treated with Ciprofloxacin the follow-up after 72 hrs. had a low performance, because only 40.0% of the persons treated could be controlled, and all had negative results. However in the one-year control, loss was only 24%, with just one case of pharyngeal reinfection with *N. meningitidis* (96% efficacy).

According to analysis of the simple table, the relative risk of pharyngeal carriage of meningococcus for the untreated study group was 4.0 ( $0.97 < RR < 16.55$ ) compared to those treated with Rifampin, and 10.0 ( $1.11 < RR < 90.26$ ) compared to those treated with Ciprofloxacin. 95% interval of reliability.

## **DISCUSSION:**

This study sought to compare the pharyngeal carriage of meningococcus in a risk group, like close contacts of an index case, with previous studies carried out in the general population from 1 to 19 years of age. We also wanted to make an impartial

evaluation of the efficacy of chemoprophylaxis with Rifampin and compare it to Ciprofloxacin.

To obtain reliable laboratory results we used a double pharyngeal smear that has a demonstrated efficacy of 95% in finding the germ compared to 71% when only one culture is used.

Comparing our results with those of the 1987 study, no significant differences in pharyngeal carriage of the meningococcus in general are seen, or of the epidemic strain (B.15 1.3), despite the different characteristics of the two groups and the fact they were carried out in different epidemic periods.

It does call one's attention, however, that the group from 1 to 5 years of age was the group that showed a higher proportion of Lactamic Neisseria. If we consider that the highest rate of frequency of Meningococcal Meningitis during the period of the study also appeared in that age group, with a pharyngeal carriage of meningococcus of 62.5% when they contracted the disease, we could propose that the high frequency of Lactamic Neisseria observed constituted a protective factor in the contacts studied, as has been proposed in other works done previously.

Rifampin in our medium continues to be an efficient way of eliminating the condition of carrier from the patient and his contacts. This contrasts with international publications that show efficacy for this drug of no more than 60%. Ciprofloxacin, besides greater efficacy, has the advantage of being used in one dose which generates higher adhesion to treatment at a lower cost.

In the last few years we have been exposed to a growing rate of Tuberculosis in the region and in Chile in general. Rifampin is an important support for that disease, with the drawback that it rapidly generates bacterial resistance to the drug. Regarding the Quinolones, there are various foreign experiments that have questioned the supposed harmful effect of these drugs when used in children, even in prolonged treatments.

In light of these considerations the use of Ciprofloxacin could be proposed as the drug of choice for chemoprophylaxis of contacts infected with Neisseria meningitidis of any age.

Chemoprophylaxis with Rifampin, in two daily doses for two days as we used it, was very effective and it is not necessary, therefore, to extend it to four days which is the local pattern.

The latter pattern is due to the importance of *Haemophilus influenza* type B as a germ that causes meningitis, although there have already been experiments, with limited numbers of volunteers, that show that a pattern of two days of treatment with Rifampin can be just as useful in the pharyngeal eradication of this germ.

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MINISTRY OF HEALTH

Support PAHO / WHO / AID / General Directorate of Epidemiology

C E R T I F I C A T E

This is granted to Dr. Ricardo Bustamante Risco

For having participated as: Speaker

In the International Seminar Workshop "PREVENTION AND SURVEILLANCE OF MENINGITIS", organized by the Health Sub-region of Tacna and General Directorate of Epidemiology of the Ministry of Health, held from October 10 to 13, 1993, with a duration of 30 hours of theoretic-practical work.

Tacna, October 13, 1993

Dr. José Ferrer Rojas  
DIRECTOR GENERAL  
TACNA SUB-REGION OF HEALTH

Dr. Mario Chuy Chiu  
DIRECTOR GENERAL  
EPIDEMIOLOGY MIN. HEALTH

MINISTRY OF HEALTH

Support PAHO / WHO / AID / General Directorate of Epidemiology

C E R T I F I C A T E

This is granted to Marcela Del Pilar Martínez Marco

For having participated as: Speaker

In the International Seminar Workshop "PREVENTION AND SURVEILLANCE OF MENINGITIS", organized by the Health Sub-region of Tacna and General Directorate of Epidemiology of the Ministry of Health, held from October 10 to 13, 1993, with a duration of 30 hours of theoretic-practical work.

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DIRECTOR GENERAL  
EPIDEMIOLOGY MIN. HEALTH

Chilean  
Health Seminar  
CHILEAN HEALTH ASSOCIATION

SANTIAGO, NOVEMBER 16, 1993

DR.  
RAMSES AGUIRRE MONTOYA  
DIRECTOR  
IQUIQUE HEALTH SERVICE  
-----

Dear Dr. Aguirre:

The board of the Chilean Health Association requests that you authorize Dr. Ricardo Bustamante, Pediatrician in charge of the field studies of the American anti-meningococcal B vaccine carried out in Iquique, to participate on the Commission on meningococcal meningitis B that the Chilean Health Association has formed for the Seventh Chilean Health Seminar that will be held on November 26 from 2:00 to 5:00 o'clock in the Events Center of the University of Santiago.

It would be advisable for Dr. Bustamante to attend a preparatory meeting of the Commission that is planned for the day before.

Thank you for your attention and cooperation.

Sincerely yours,

DR. MARIANO REQUENA B.  
PRESIDENT

Chilean Association of Infectious Disease

Santiago, August 16, 1994

DEAR DR. RICARDO BUSTAMANTE:

The Chilean Association of Infectious Disease met in November 1990 to systematize the experience acquired by different national work groups on the subject of Acute Bacterial Meningitis. A multidisciplinary Workshop was held for two days which was attended by specialists in Infectious Diseases, clinical Microbiologists, Epidemiologists and Physicians specialized in intensive care, a Neonatologist, a Neurosurgeon and a Neuroradiologist were especially invited to address topics in their special areas of expertise in a well-founded manner.

RECOMMENDATIONS FOR DIAGNOSIS, TREATMENT AND PREVENTION of ACUTE BACTERIAL MENINGITIS resulted from this Workshop, which were published in the REVISTA CHILENA DE INFECTOLOGIA (Chilean Journal of Infectious Diseases) and distributed widely as a monograph published with the cooperation of the BETA BIOCHEMICAL INSTITUTE during 1991.<sup>1</sup>

From that time until the present new information and challenges have arisen in this pathology like the proliferation in Chile of resistant strains of *S. pneumoniae* and *N. meningitidis*, the use of new therapeutic arms (corticosteroid therapy, new cephalosporines, etc.), an epidemic of Meningococcal Disease and a wide-ranging discussion of applicable vaccines in : Acute Bacterial Meningitis. All of these developments provide more than enough justification for our meeting again to find out about the progress made by the different groups and to update our recommendation on the matter.

Your work group has been selected by the coordinators of this activity to participate in this new workshop in light of the experience you have acquired on the subject. To make the Workshop more operative we would like to ask you to appoint a representative of the group to give your opinion on the day of the event.

We are enclosing a questionnaire about the topics that will be submitted for discussion so that every new recommendation will be based on national experience, not just on information acquired from the literature.

The following Institutions have been invited to attend the SECOND WORKSHOP ON ACUTE BACTERIAL MENINGITIS:

Hospital Regional de Iquique  
Hospital van Buren de Valparaíso  
Hospital Gustavo Fricke de Viña del Mar  
Hospital Regional de Talca  
Hospital Regional de Concepción  
Hospital de Talcahuano  
Hospital Regional de Temuco  
Hospital Regional de Valdivia  
Hospital Regional de Puerto Montt

In the Metropolitan Region:

Hospital de Enfermedades Infecciosas Lucio Córdova  
Hospital Exequiel Gonzalez Cortés  
Hospital Felix Bulnes  
Hospital Luis Calvo Mackenna  
Hospital Roberto del Río  
Hospital San Borja Arriarán  
Hospital San Juan de Dios  
Hospital Sótero del Río  
Hospital de la Pontificia Universidad Católica de Chile  
Hospital Militar  
Instituto de Salud Pública

Thank you for your willingness to cooperate with the Chilean Association of Infectious Disease:

Dr. Enna Zunino M. and Dr. José Cofré G.

Coordinators of the Workshop.

Chilean Association of Infectious Diseases

Santiago, October 13, 1994

DR. Ricardo Bustamante  
DEPARTMENT OF Pediatrics  
HOSPITAL Dr. E. Torres de Iquique

Dear Dr.:

As the coordinator of the Second Workshop on Acute Bacterial Meningitis organized by the Chilean Association of Infectious Disease, I would like to inform you of the following:

- the date has been changed to Saturday, December 3 because of the availability of the venue.
- the meeting will be held in Viña del Mar, at CONFERENCE TOWN, a comfortable convention center located in Reñaca.
- the approximately 40 participants will be transported from Santiago on a bus that will leave at 8:00 A.M. and arrive in Viña del Mar at approximately 10:00 A.M.
- the working meeting will last from 10:30 to 19:00 hours including lunch and coffee breaks. - We are considering a closing dinner, which might be voluntary.

In principle the return to Santiago will be at 19 hours unless a dinner is held.

- This activity is being sponsored by Hoechst Chile.
- It is essential, for organization purposes, for you to confirm the participation of a member of the Department you work in and the name of the appointed colleague before October 21 by fax addressed to our secretary, Mrs. Dalma Domic.

PAN AMERICAN HEALTH ORGANIZATION

Pan American Health Office, Regional Office of the

WORLD HEALTH ORGANIZATION

FACSIMILE

FAX N°.: 682      DATE:10.21.93      DESTINATION: Iquique      Pg. 1 of 1  
FROM: Dr. Gustavo Mora, FWR Chile  
TO: Dr. Ramsés Aguirre, Director SS  
SUBJECT: 2nd Chilean Congress of  
Epidemiology

Text:

We hereby certify that Dr. Ricardo Bustamante, Coordinator of the Project to Test Vaccination for Meningitis B, in Iquique, has been invited to participate in the 2nd Chilean Congress of Epidemiology, that will be held in Santiago between October 26 and 29, 1993.

The PAHO/WHO will only be responsible for the Dr. Bustamante's registration expenses at the congress.

The above does not include transportation expenses or per diem allowance.

Dr. Gustavo Mora  
Representative PAHO/WHO in Chile

cc: Dr. Ricardo Bustamante

PREVALENCE OF CARRIAGE OF NEISSERIA  
MENINGITIDIS IN A GROUP OF 1017 PEOPLE BETWEEN 1 AND 21 YEARS OF  
AGE IN THE CITY OF IQUIQUE AND THEIR COMPARISON WITH THE SAME  
STUDY CARRIED OUT IN AUGUST 1987 DURING THE EFFICACY STUDY OF THE  
MENINGOCOCCAL VACCINE.

1- BACKGROUND :

-----

In August of 1987 in the city of Iquique, Pozo Almonte and Pica the vaccine being studied was given for Meningococcal Meningitis to the whole population from 1 to 19 years of age that volunteered to receive it, after they had signed a letter of consent as required by the protocol.

A follow-up group was formed of 1017 children whose ages varied between 1-19 years.

A blood sample was taken from these children to measure the response of antibodies to the vaccine, and a pharyngeal smear was also taken to study the prevalence of carriage of Neisseria meningitidis at that time.

The vaccine showed an efficacy of 51%, so another study will have to be done in the future.

Regarding the prevalence of carriage, it was found that in 1987 in the middle of an epidemic of meningitis there were 11.5% carriers of Neisseria Meningitidis, and 1.9% of the epidemic strain B:15 1.3 in the age group from 1 to 19 years, and that Lactamic Neisseria (protective) decreased as the person aged, whereas N. meningitidis increased with age and was greater in children from 10 to 13 years.

2 - POSSIBLE PROTOCOL :

-----

A double pharyngeal smear will be taken from 1017 children considering the following criterion for inclusion (to obtain similar samples to the ones taken in 1987).

A - Age group : 1 to 19 years

B - Number of pharyngeal smears by age group.

1-5 yrs.	= 523 x 2	1046
6-9 yrs.	= 140 x 2	280
10-13 yrs.	= 102 x 2	204
14-19 yrs.	= 252 x 2	504
	-----	----
Total	1017	2034

C - Educational establishments : the same establishments selected in 1987, with similar characteristics.

<u>Educational estab.</u>	<u>age group</u>	<u>total samples</u>
J.I. Payasito (Junji)	3 to 6 yrs.	47
J.I. Lobito Feroz (Junji)	1 to 5 years	70
J.I. Guayabito (Junji)	2 to 5 years	72
J.I. Emita (Private)	1 to 5 years	37
C. Hispano Britanico (Priv.)	2 to 5 years	37
	6 to 11 years	52
Esc. E-70 (Primary)	5 to 14 years	205
Liceo A-7 (High School)	13 to 19 years	260
Outpatient clinics	1 to 2 years	236

Duration of study : Two months (March - April 1995)

Possible date planned for taking samples : Monday 27 to Friday, April 7 this year.

Human Resources

-----

3 Nursing Teams (sos,)

Each Team will be made up of 1 Nurse + 1 Paramedic Auxiliary.  
(fundamentally from Primary Health Care).

The reception capacity for samples in our laboratory will be 300 PS per day so each team should take 100 PS (50 doubles) per day.

Seven working days are planned per team.

The backup team will fill in if samples are missing in the days after the work has been finished.

# SCHEDULE

=====

DATE	EDUC. EST.	AGE G.	NUMBER PS	TOTAL
------	------------	--------	-----------	-------

March

Monday 27

Tuesday 28

Wed. 29

Thurs. 30

Fri. 31

April

Mon. 3

Tues. 4

Monday 3 - Fri., April 7    Outpatient Clinics

Atacama Health Service

Ministry of Health

Pan American Health Organization

**CERTIFICATE**

This certificate is granted to

Dr. Ricardo Bustamante R.

for his participation as the **Main Author** of the work called

Study of pharyngeal carriage of Neisseria meningitidis in  
contacts of patients with meningococcal meningitis in Iquique

presented at the III Public Health Seminar of the Northern  
Regions.

Celsa Carmona Garcia  
Head of Dept. of Epidemiology  
and Research  
Atacama Health Service

Dr. Alberto Roblas Pantoja  
Director  
Atacama Health Service

Copiapó, August 24 to 26, 1994.-

Atacama Health Service

Ministry of Health

Pan American Health Organization

**CERTIFICATE**

This certificate is granted to

Dr. Ricardo Bustamante R.

for being a **Participant** in the III Public Health Seminar of the Northern Regions.

Celsa Carmona Garcia  
Head of Dept. of Epidemiology  
and Research  
Atacama Health Service

Dr. Alberto Roblas Pantoja  
Director  
Atacama Health Service

Copiapó, August 24 to 26, 1994.-

**XX NATIONAL CONGRESS OF PEDIATRICS**  
Concepción, November 16 to 19, 1994

Information about speaker

1. NAME: Ricardo Bustamante Risco TELEPHONE: 441636 FAX: (057) 426014

ADDRESS: Alberto Gennari 2122 CITY: Iquique

2. FOR ORAL PRESENTATION: X WILL USE SLIDES: YES  
FOR PANEL PRESENTATION

Authors: Ricardo Bustamante R. Marcela Martínez M.  
Workplace: Research Lab. of Meningococcal Disease Iquique Hospital

Title : Pharyngeal carriage of Neisseria meningitidis in  
contacts of patients with Meningococcal Meningitis

During May 1992 and May 1993 pharyngeal carriage of Neisseria meningitidis was evaluated among the contacts of those patients that presented meningococcal meningitis.

The objective was to determine the prevalence of pharyngeal carriage of group B meningococcus in a high-risk population, verify the efficacy of Ciprofloxacin and Rifampin as chemoprophylactics and establish a comparison with similar previous studies. Of 872 contacts recorded between under one year and over 51 years, the highest rate of prevalence was observed in those under 19 years of age compared to the total of positive pharyngeal carriers for meningococcus in general, which constituted only 10% of the total of the sample. The prevalence of the epidemic strain between one and 19 years of age did not differ noticeably from the prevalence obtained for the same age group in a study done in 1987. (1.3% and 1.9%, respectively).

The efficacy as chemoprophylactics of Ciprofloxacin and Rifampin was high both in the immediate eradication of the meningococcus and in the low pharyngeal reinfection by this germ one year later.

It should be stated that Rifampin was used in a system of two daily doses for two days; Ciprofloxacin is given in one dose.

A more massive use of Ciprofloxacin is proposed as chemoprophylaxis in the prevention of meningococcal disease, in view of its greater efficacy, better adhesion to treatment and lower cost than Rifampin, which has the drawback of the appearance of resistant mutant strains in a country with rates of TBC that are rising, for which reason this medicine continues to have undeniable value.

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<sup>1</sup> Vol. 8, N° 2 (pp. 61-73) and Vol. 8, N° 3 (pp. 117-134) 1991.

# ANTOFAGASTA WRAIR PROJECT

## FINAL REPORT

### 1. INTRODUCTION:

The Meningococcal Disease has an endemic behaviour and reaches an incidence rate of 1-2 cases per 100,000 inhabitants. This incidence rate has been progressively increasing in Antofagasta since 1987 and has reached 17 cases per 100,000 inhabitants in 1992. The above situation has caused concern among health authorities both at the regional and at the national levels. Among others, one of the strategies to fight this disease, has been the search for an effective vaccine against Meningococcus Serogroup B which is responsible for the epidemic outbreak in our city. To that effect, the implementation of a Research Project which would permit the utilization in our city of Phase II of effectiveness of a vaccine elaborated by the United States Walter Reed Institute was carried out in conjunction with the above-mentioned Institute.

### 2. GENERAL OBJECTIVES:

- (A) To evaluate the effectiveness of the antimeningococcus Serogroup B vaccine elaborated by the WRAIR.
- (B) To maintain an Active System of Epidemiology Vigilance of the Meningococcal Disease in Antofagasta.

### 3. PERIOD UNDER STUDY:

From 1 January 1993 till 19 June 1995.

### 4. STAFF:

Antonio Cárdenas Tadich	Physician
Mrs. Andrea Contreras Garay	Nurse
Mr. Claudio Rojas Quinteros	Medical Technician
Mrs. Rosa Rivera Aracena	Secretary

### 5. ACTIVITIES CARRIED OUT:

- (A) Characterization and preservation of C.R.L. (cephaloraquidian liquid) and blood cultures of confirmed cases and of healthy carriers.

- (B) Taking of samples of acute and convalescent sera of all confirmed cases.
- (C) Carrying out coordination and sanitary education activities at all local health sectors in relation with Meningococcal Meningitis.
- (D) Making of home visits, epidemiology surveys, and follow-up of all Meningococcal Disease cases.
- (E) Maintenance of daily computerized records, as well as files of all Meningococcal Disease cases.
- (F) Establishment of communication links with local media to allow for the insertion of the Project into the Antofagasta community.
- (G) Nomination of the Chief of the Project as President of the Regional Meningococcal Disease Committee thus establishing the coordination and insertion of the Project at all levels of local health activities.
- (H) Undertaking of three studies on healthy carriers:
  - (i) On Health Staff of the Regional Hospital and of the Antofagasta Clinic in 1993.
  - (ii) At School D-65 in 1994.
  - (iii) In 1995, on the pediatric population of Antofagasta. Samples from 1,000 children were taken.
- (I) To date and since May 1994, a follow-up of 18 healthy treated carriers has been made in order to verify an eventual recolonization.
- (J) Development of a new Meningococcal chemoprophylaxis plan for the region which simplified the previous plan and made it more effective.
- (K) Presentation of three research papers on Meningococcal Disease in Antofagasta at the XX Chilean Pediatrics Convention.
- (L) One of these papers will be included in the Chilean Pediatrics Magazine.
- (M) Creation of Treatment and Transfer Regulations. Regional Meningococcal Disease.

Note: Protocols and Certificates of Activities are included in the Appendices Section.

## 6. STATISTICAL SUMMARY

Table No 1 Meningococcal Disease: Distribution and Incidence of Cases.

Y E A R	NUMBER OF CASES	INCIDENCE *
1993	24	10.1
1994	19	8.0
1995	08	3.4**

\* Cases per 100,000 inhabitants

\*\* Till 15 May 1995

Table No 2 Meningococcal Disease: Distribution by Chronological Age

AGE GROUP	1993		1994		1995**	
	No	Incidence*	No	Incidence	No	Incidence
< 1 year	7	11.8	2	33.6	1	
12 - 23 months	3	51.5	1	17.1	1	
2 - 5 years	3	14.2	8	38.0	1	
6 - 14 years	5	17.2	5	17.2	4	
15 years and more	6	3.6	3	1.8	1	
T O T A L	24	10.1	19	8.0	8	

\* Cases per 100,000 inhabitants

\*\* Till 15 May 1995

Table No 3 Meningococcal Disease: Distribution by Sex during the Period under Study

S E X	1993		1994		1995*	
	No	%	No	%	No	%
Masculine	14	58.3	13	68.4	3	37.5
Feminine	10	41.7	6	31.6	5	62.5
T O T A L	24	100	19	100	8	100

\* Till 15 May 1995

Table No 4 Lethality according to Age Group and Years under Study

AGE GROUP	CASES		DEATHS		LETHALITY	
	1993	1994	1993	1994	1993	1994
1 year	7	2	2	1	28.5	50
12 - 23 months	3	1	1	0	33.3	0
2 - 5 years	3	8	2	0	66	0
6 - 14 years	5	5	1	0	20	0
15 years and more	6	3	2	0	33	0
T O T A L	24	19	8	1	33	5.8

NOTE: No deceases recorded during 1995 to date.

Table No 5      Distribution of Cases by Clinical Form and Lethality

CLINICAL FORM	CASES		DEATHS		LETHALITY	
	1993	1994	1993	1994	1993	1994
Meningitis	16	15	1	0	6.25	0
Mixed	4	1	3	0	75	0
Meningococemia	4	3	4	1	100	33
T O T A L	24	19	8	1	33	5.8

NOTE: No deceases recorded during 1995 to date.

Table No 6      Distribution by Months

M O N T H S	1993 No of Cases	1994 No of Cases	1995 No of Cases
January	2	1	1
February	1	3	3
March	2	1	2
April	5	1	0
May	1	1	2
June	2	0	
July	3	0	
August	2	2	
September	2	2	
October	1	3	
November	2	4	
December	1	1	
TOTAL	24	19	8

Table Nº 7      Results of the Study made on Healthy Carriers  
in Pediatric Population. Antofagasta, 1995

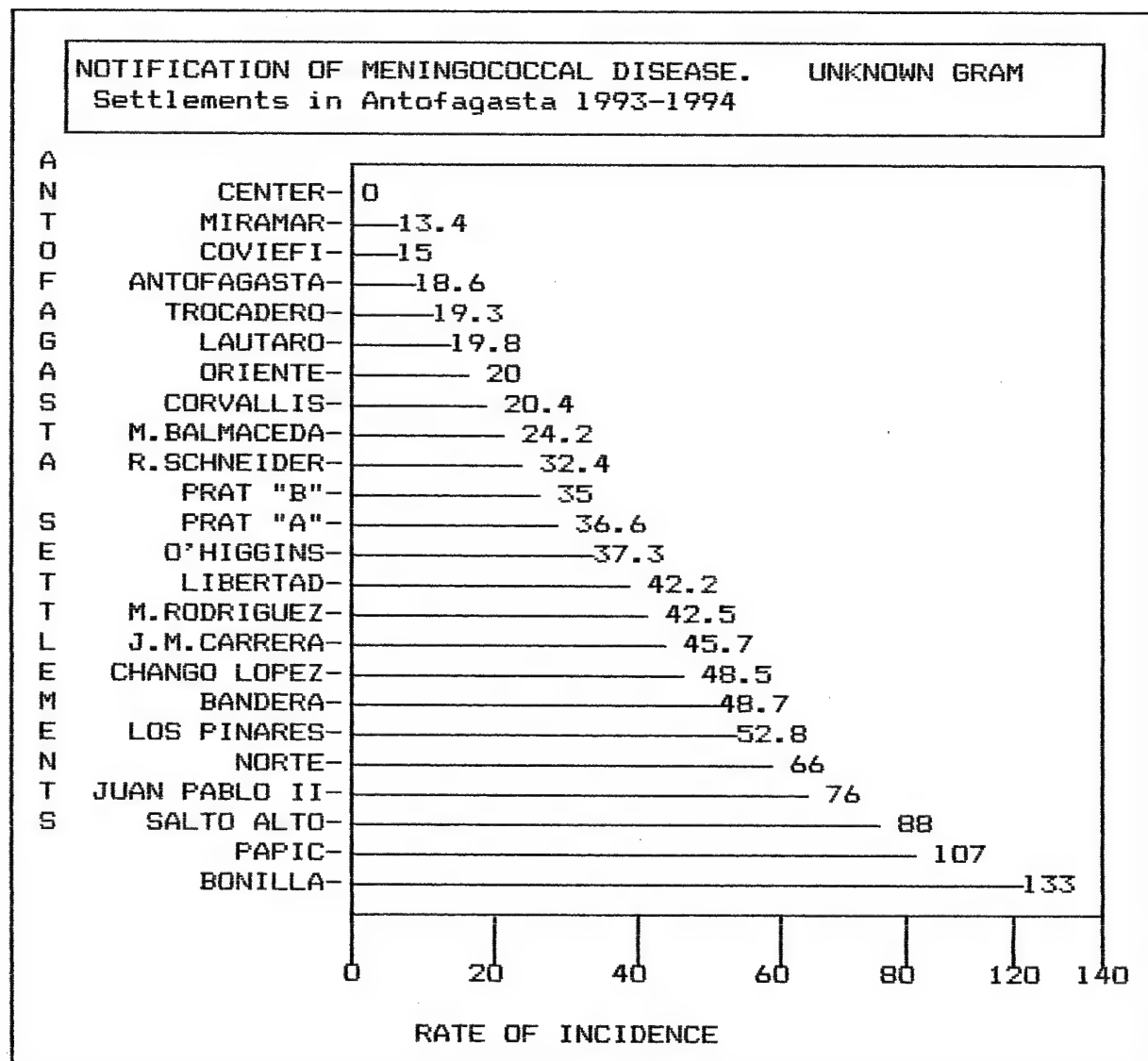
AGE GROUP	NEGATIVE		N. MENING.		N. MENING.GROUP B	
	Nº	%	Nº	%	Nº	%
1 - 5 N : 342	323	94.4	20	5.8	16	4.6
6 - 9 N : 190	182	95.7	8	4.2	8	4.2
10 - 13 N : 207	197	95.1	11	5.3	10	4.8
14 - 19 N : 266	247	92.8	21	7.9	19	7.1
T O T A L N: 1,005	949	94.4	60	6.0	53	5.2

Chart Nº 1:     Distribution of Acute Bacterial Meningitis by  
                 Aetiology

DISTRIBUTION OF MENINGITIS BY AETIOLOGY  
Antofagasta 1993 - May 1995

	H. INFLUENZAE (11.4%)
	S. NEUMONIA (8.0%)
N. MENINGITIDS (58.8%)	
	UNKNOWN GERM (22.9%)
	Total Cases: 88

Chart Nº 2: Distribution of Meningococcal Disease Cases by Districts of Antofagasta



## 7. APPENDICES

- (A) Consolidation of Acute Bacterial Meningitis Cases in Antofagasta during the period under study included in our data bank.
- (B) New Regional Chemoprophylaxis Plan.
- (C) Treatment and Transfer Regulations for Meningococcal Disease Cases in the Region.
- (D) Protocols and Summary of Research Studies and Certificates of Participation.
- (E) Summary of press articles related to the WRAIR Project in Antofagasta.

## A P P E N D I C E S

**CONSOLIDATION OF  
ACUTE BACTERIAL MENINGITIS CASES  
IN ANTOFAGASTA DURING THE PERIOD  
UNDER STUDY**

Republic of Chile  
MINSAL  
Health Service Aphtha  
Wrair Project

MENINGITIS CASES 1993

CASE NO	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI **	CULTURE		LATEX	GRAM	C/D ***
							CSF	HEM			
01	C	Johan Carvajal	02/01/93	7 months	Meningitis	Yes	+	-	none	+	ANS***
02	C	Diego Pizarro	04/01/93	1 yr.2 m.	Meningitis	Yes	+	-	+	+	ANS
04	S	Sixto Beltrán	31/01/93	13 years	Unknown	Yes	-	-		-	ANS
05	ALT	Valeria Muñoz	05/02/93	1 month	Meningitis	Yes	-	-	+	+	ANS
07	C	Luis Muñoz	01/03/93	6 months	Meningitis	Yes	+	-	+	+	ANS
08	C	Juan Rojas	26/03/93	11 years	M.Meningoc.	Yes	+	none	-	-	Dead
09	C	Manuel López	07/04/93	4 years	M.Meningoc.	Yes	+	none	-	-	Dead
10	ALT	Victor Cortez	07/04/93	6 years	Meningitis	Yes	-	-	-	+	ANS
11	C	Carlos Barreda	08/04/93	58 years	Meningitis	Yes	+	none	-	+	Dead
12	C	Daniela Carlo	14/04/93	1 yr.3 m.	Meningoc.	Yes	-	+	-	-	Dead
13	ALT	Juan Fernández	15/04/93	33 years	Meningitis	Yes	-	none	-	+	ANS
15	C	Mauricio Mercado	13/05/93	20 years	Meningitis	Yes	+	none	-	+	ANS
16	S	Juan Talamilla	21/05/93	1 y.11 m.	Unknown	Yes	-	-	-	-	ANS
19		Jeiny Rodríguez	02/06/93	8 years	Unknown	Yes	-	-	-	-	ANS
20	C	Guillermo Madariaga	09/06/93	47 years	M.Meningoc.	Yes	+	none	+	-	Dead
21	C	Nury Ramos	21/06/93	8 years	M.Meningoc.	Yes	+	+	+	+	ANS
22		Andrés Aguilar	27/06/93	19 years	Unknown	Yes	-	-	-	-	ANS
23	C	Patricia Carrizo	06/07/93	20 years	Meningitis	Yes	+	none	+	+	ANS
24	C	Jenny Pérez	06/07/93	27 years	Meningitis	Yes	+	none	-	+	ANS

\*\* CLI = Clinic

\*\*\* C/A = Condition at Discharge

\*\*\*\* ANS = Alive with No Sequelae

CASE NO	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI	CULTURE		LATEX	GRAM	C/D
							CSF	HEN			
26	C	Fernando González	11/07/93	3 months	M.Meningoc.	Yes	-	+	-	-	Dead
30	S	Priscila Flores	16/08/93	7 months	M.Meningoc.	Yes	-	-	-	-	Dead
31	S	Marcelo Collao	25/08/93	5 years	Unknown	Yes	-	-	-	-	ANS
32	SOS	Catalina Martínez	26/08/93	11 days	Unknown	Yes	-	-	-	-	ANS
33	C	Nicol Tapia	31/08/93	3 yrs.8m.	M.Meningoc.	Yes	+	+	+	+	Dead
35	C	Juan Sepúlveda	06/09/93	8 years	Meningitis	Yes	+	-	-	-	ANS
37	C	Nicol Fontalba	30/09/93	11 months	Meningitis	Yes	+	-	-	-	ANS
38	C	Cristián Araya	11/10/93	11 months	Meningitis	Yes	+	-	-	-	ANS
40	C	Olga Jacobs A.	02/11/93	6 yrs.7m.	Meningitis	Yes	+	-	-	-	ANS
41	C	Guillermo Cuevas	03/11/93	1 year	Meningitis	Yes	+	-	-	-	ANS
43	S	Verónica Villaroel	02/12/93	29	Unknown	Yes	-	none	-	-	ANS
44	S	Dafne Aguilera A.	16/12/93	1 year	Unknown	Yes	-	-	-	-	ANS
45	C	Carolina Maya A.	17/12/93	5 years	Meningitis	Yes	+	-	-	+	ANS

1994

CASE NO	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI	CULTURE		LATEX	GRAM	C/D
							CSF	HEM			
46	S	José Astorga Morales	02/01/94	6 months	Unknown	Yes	-	-	-	-	ANS
47	Con	Juritza Aro Vergara	09/01/94	2 years	Haem.		-	-	+	+	ANS
48	S	Melisa Aguilera Alcaíno	10/01/94	8 months	Unknown	Yes	-	-	-	-	ANS
49	Con	Francisca Ramírez Lembech	15/01/94	9 years	Meningitis	Yes	+	none	+	+	ANS
50	S	Isaack Rebolledo Gómez	26/01/94	7 years	Unknown	Yes	-	none	-	-	ANS
51	Con	Guillermo Guzmán Tapia	03/02/94	4 years	Meningococ.	Yes	-	+	-	-	ANS
52	Con	Catalina Sáez Espinoza	19/02/94	5 months	Meningococ.	Yes	+	-	-	-	Dead
53	Con	Reinaldo Rocha Vega	20/02/94	39 years	Unknown	Yes	-	-	-	-	ANS
54	S	Fernando Bravo Palacios	25/02/94	10 years	Meningococ.	Yes	+	-	-	-	ANS
55	C	Fabrizio González Carreño	07/03/94	2 years	Meningococ.	Yes	+	-	-	-	ANS
56	C	Verónica Jiménez Alarcón	20/03/94	39 years	Haem.	Yes	-	none	+	-	ANS
57	S	Juan Carrizo Collao	25/03/94	13 years	Unknown	Yes	-	-	-	-	Dead
58	C	Silvia Janet Marín	28/03/94	9 months	Haem.	Yes	+	none	+	+	ANS
59	S	Marisol Zamora González	03/04/94	10 years	Unknown	Yes	-	-	-	-	ANS
60	S	Jessica Barraza.	20/04/94	6 years	Unknown	Yes	-	-	-	-	ANS

CASE No	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI	CULTURE		LATEX TEST	GRAM TEST	C/D
							CSF	HEM			
61		Juan Molina Maturana	24/04/94	1 yr.2 m.	Streptoc.	Yes	+	-	+	+	ANS
62	C	Luis Ramos F.	30/04/94	11 months	Haem.	Yes	-	-	+	+	ANS
63	C	Horacio Alfaro M.	30/04/94	4 years	Meningococ.	Yes	+	none	-	+	ANS
64		Juan Muñoz M.	04/05/94	2 yrs.7m.	Haem.	Yes	+		+	-	ANS
65	C	Pedro Jorquera D.	05/05/94	2 months	Streptoc.	Yes	+	-	none	+	Died on 20/05/94
66		Karen Rojas Rojas	18/05/94	12 years	Unknown	Yes	-	-	-	-	ANS
67		Silvia Palma Rivera	25/05/94	2 yrs.9m.	Meningococ.	Yes	-	-	-	+	ANS
68		Renato Salas Bonkowsky	07/06/94	1 yr.10m.	Haem.	Yes	+	-	+	-	ANS
69		Jesús Gallardo Eissman	23/06/94	12 years	Streptoc.	Yes	+	-	none	+	ANS
70		Stefhanie González	10/07/94	8 months	Haem.	Yes	+	+	+	+	ANS
71		Mario Núñez Núñez	13/07/94	5 yrs. 5m	Haem.	Yes	+	-	+	-	ANS
72		Lester Avila Pulgar	13/08/94	5 yrs. 9m	Meningococ.	Yes	-	-	-	+	ANS
73		Pedro Vásquez Neira	13/08/94	1 month	E. Coli	Yes			-		ANS
74		Carlos Bahmondes Urrutia	14/08/94	13 years	Streptoc.	Yes	+	none	-	+	ANS
75		Julio Sepúlveda Bravo	15/08/94	36 years	Streptoc.	Yes	+	none	+	+	ANS
76		Luis Suárez	15/08/94	11 days	Viral?	Yes	-	-	-	-	ANS
77		Marta Iribarren	17/08/94	63 years	Unknown G.	Yes	-	-	-	-	Died on 24/08/94
78		N.N. Sánchez	23/08/94	1 day	Strept. B	Yes	+		+	+	ANS
79		Cristóbal Bolado Cortés	24/08/94	11 days	Strept. A	Yes	+		+	+	Died on 25/08/94

CASE NO	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI	CULTURE		LATEX TEST	GRAM TEST	C/D
							CSF	HEN			
80	C	Luis Vilches Vilches	31/08/94	13 years	Meningococ.	Yes	-	-	-	+	ANS
81	S	María Martínez Vilches	01/09/94	5 yrs. 5m	Unknown G.	Yes	-		-	-	ANS
82	C	Javier Escudero Pastene	16/09/94	4 years	Meningococ.	Yes	-	+	-	-	ANS
83	C	Carlos Hartad Morla	21/09/94	53 years	Meningococ.	Yes	-	none	+	+	ANS
84	C	Jorge Calderón	08/10/94	16 years	Meningococ.	Yes	+	none	+	+	ANS
85	C	Bernabé Alfaro González	15/10/94	12 years	Meningococ.	Yes	-	-	-	+	ANS
86	C	Francisca Tirado Tirado	25/10/94	8 months	Meningococ.	Yes	+	-	+	+	ANS
87	C	Leonardo Contreras González	06/11/94	2 yrs. 8m	Meningococ.	Yes	-	-	-	+	ANS
88	C	Juan Zepeda Cisternas	14/11/94	29 years	Meningococ	Yes	+	none	-	-	ANS
89	C	Richard Tapia Guerrero	14/11/94	8 years	Meningococ	Yes	-	+	-	-	ANS
90	C	Carolina Ramírez Casa	29/11/94	1 yr. 10m	Meningitis	Yes			-	+	ANS
91	C	Williams Castillo Iturra	15/12/94	3 years	Meningococ.	Yes	+	-	IS*	+	ANS
92	C	Luis Castillo Herrera	30/12/94	1 yr. 3m	Haem.	Yes	+	-		+	Hosp.

\* Insufficient Sample

CASE NO	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI	CULTURE		LATEX TEST	GRAM TEST	C/A
							CRL	HEM			
80		Luis Vilches Vilches	31/08/94	13 years	Meningococ.	Yes	-	-	-	+	ANS
81		María Martínez Vilches	01/09/94	5 yrs. 5m	Unknown G.	Yes	-		-	-	ANS
82		Javier Escudero Pastene	16/09/94	4 years	Meningococ.	Yes	-	+	-	-	ANS
83		Carlos Hartad Morla	21/09/94	53 years	Meningococ.	Yes	-	none	+	+	ANS
84		Jorge Calderón	08/10/94	16 years	Meningococ.	Yes	+	none	+	+	ANS
85		Bernabé Alfaro González	15/10/94	12 years	Meningococ.	Yes	-	-	-	+	ANS
86		Francisca Tirado Tirado	25/10/94	8 months	Meningococ.	Yes	+	-	+	+	ANS
87		Leonardo Contreras González	06/11/94	2 yrs. 8m	Meningococ.	Yes	-	-	-	+	ANS
88		Juan Zepeda Cisternas	14/11/94	29 years	Meningococ.	Yes	+	none	-	-	ANS
89		Richard Tapia Guerrero	14/11/94	8 years	Meningococ.	Yes	-	+	-	-	ANS
90		Carolina Ramírez Casa	29/11/94	1 yr. 10m	Meningitis	Yes			-	+	ANS
91		Williams Castillo Iturra	15/12/94	3 years	Meningococ.	Yes	+	-	IS*	+	ANS
92		Luis Castillo Herrera	30/12/94	1 yr. 3m	Haem.	Yes	+	-		+	Hosp.

\* Insufficient Sample

1995

CASE NO	CLS	NAME	DATE OF ADMISSION	AGE	AETHIOLOGY	CLI	CULTURE		LATEX TEST	GRAM TEST	C/D
							CSF	HEM			
93	C	Sara Inostroza Meléndez	22/01/95	50 years	Unknown G.	Yes	-	none	-	-	Died on 28/01/95
94	C	Pablo Gárnica Trinick	22/01/95	6 yrs. 3m	M.Meningoc.	Yes	-	-		+	ANS
95	C	Jocelyn Villanueva Villagrán	01/02/95	1 yr. 7m	M.Meningoc.	Yes	+	-	-	+	ANS
96	C	Patricia Vicencio Espinoza	03/02/95	2 years	M.Meningoc.	Yes	-	-	+	+	ANS
97	C	Fresia Cortés	18/02/95	45 years	M.Meningoc.	Yes	+		+	+	ANS
98	C	Carolina González Varas	10/03/95	14 years	M.Meningoc.	Yes	+	-	+	+	ANS
99	C	Janssen Rojas Díaz	16/03/95	6 months	M.Meningoc.	Yes	+		+	-	ANS
100	C	Darwin Avendaño	24/03/95	60 years	Purulent M.	Yes	-	none	-	-	Died on 29/03/95
101	C	Nataly Cisterna Iriarte	12/04/95	12 years	Unknown M.G.	Yes	-	-	-	-	ANS
102	C	Francisco Campillay Soza	24/04/95	3 yrs. 3m	Haem.	Yes	+	none	+	-	ANS
103	C	Melisa Tobar Zárate	02/05/95	7 years	M.Meningoc.	Yes	-	none	-	+	ANS
104	C	Daniel Villacura	07/05/95	6 years	M.Meningoc.	Yes	-	none	-	+	ANS

**CHEMOPROPHYLAXIS FOR  
MENINGOCOCCAL DISEASE**

CHEMOPROPHYLAXIS PROPOSAL FOR MENINGOCOCCAL DISEASE  
WRAIR PROJECT 1993

Mrs. Andrea Contreras

Dr. Antonio Cárdenas

Chemoprophylaxis shall be made through RIFAMPIN for patients UNDER 17 years and through CIPROFLOXACIN for those OVER 17 years.

(A) - DOSAGE

1 - NEONATES

Rifampin 5 mg. per kilogram of weight, per day, divided in two daily doses and for TWO DAYS, in syrup.

2 - CHILDREN OF BETWEEN 1 MONTH AND 6 YEARS 11 MONTHS OF AGE.

Rifampin 10 mg. per kilogram of weight, per day, divided in two daily doses and for TWO DAYS, in syrup.

3 - CHILDREN OF BETWEEN 7 YEARS AND 16 YEARS 11 MONTHS OF AGE.

Rifampin 10 mg. per kilogram of weight, per day, divided in two daily doses and for TWO DAYS, in capsules.

4 - SUBJECTS OVER 17 YEARS OF AGE

Ciprofloxacin: in a single dose of 500 mg., in capsules.

(B) - CONTRAINDICATIONS FOR BOTH ANTIBIOTICS

1. Pregnant women at any period of gestation
2. Nursing mothers
3. Active and chronic hepatitis, hepatic cirrhosis
4. Allergy to any of the two

In the above cases use: Ceftriaxone 250 mg., intramuscular, in a single dose. In the case of contraindication in children use: Ceftriaxone, 125 mg., intramuscular, in a single dose.

(C) - PRESENTATION OF THE PRODUCTS

1. - Rifampin

- (a) Syrup; Chilean trade name: Rifaldin one flask = 50 ml. 5 cc = 100 mgr. of Rifampin.
- (b) Capsules of 150 mg.

2. - Ciprofloxacin

Capsules of 250-500-750 mgs. Chilean trade name Bay cip.

3. - Ceftriaxone  
Chilean trade name: Acantex  
Presentation: flask-ampule: 500 mgr.  
Presentation: flask-ampule: 1 gr.

(D) - GUIDE FOR THE USE OF Rifampin.

1. For children under 6 years 11 months, it shall be used in syrup.

(a) Shake before using.

(b) The measure-cap has marks for 2.5 cc - 5 cc - 10 cc.

The 2.5 cc measure = 50 mgr. of Rifampin

The 5 cc measure = 100 mgr. of Rifampin

The 10 cc measure = 200 mgr. of Rifampin

(c) Dosage according to child's weight:

10 mgr per kilogram per day = 0.5 cc per kilogram per day.

5 - 6 kg. = 1.5 cc every 12 hours for 2 days

7 - 8 kg. = 2 cc every 12 hours for 2 days

9 - 11 kg. = 3 cc every 12 hours for 2 days

12 - 14 kg. = 3.5 cc every 12 hours for 2 days

15 - 17 kg. = 4.5 cc every 12 hours for 2 days

18 - 20 kg. = 5 cc every 12 hours for 2 days

21 - 23 kg. = 6 cc every 12 hours for 2 days or  
1 capsule every 12

hours, if  
possible.

In the above indications we have provided cover for children of up to 7 years of age. We are of the opinion that over that age the child is able to ingest capsules.

1. For children over 7 years and adults.

24 - 30 kg. = 1 capsule every 12 hours for 2  
days

31 - 40 kg. = 1.5 capsule every 12 hours for 2  
days

41 - 60 kg. = 2 capsules every 12 hours for 2  
days

NOTE:

1. It is possible that the prohibition to use CIPROFLOXACIN in children will be released.
2. It is suggested that a study be made on sensitivity to SULFADIAZINE.

APHTHA HEALTH SERVICE  
MENINGITIS LABORATORY  
WRAIR PROJECT

FULMINANT  
MENINGOCOCCEMIA

TREATMENT AND TRANSFER  
REGULATIONS

DR. T. VERDEJO A.  
DR. A. CARDENAS T.

## **FULMINANT MENINGOCOCCEMIA**

### **1. INTRODUCTION**

Since 1987, the II Region has been affected by an unexpected increase in the number of Meningococcal Disease cases, which has been a cause of concern to local health authorities who have implemented several strategies to diminish its propagation. During the present year we have observed a decrease in the incidence rate but a considerable increase in the lethality of the disease for which reason we have deem it advisable to review, update and regulate the diagnosis and treatment of the septic shock provoked by Meningococcal Disease. Fulminant Meningococemia is by far the foremost cause of septic shock in the children of Antofagasta. It is characterized by its very fast evolution which has been supported by local studies that determined that all deaths of children occurred within the first 24 hours of hospitalization. The same seems to be valid for adults.

### **2. DEFINITION**

An acute condition, violent, of rapid establishment, great lethality, provoked by the invasion of the organism by Neisseria Meningitidis, characterized by high fever, seriously affecting the general state of the patient and with extensive purpuric exanthem.

Certain diagnosis is obtained through + blood cultures, but in view of the vicious virulence of the condition, clinical suspicion should be sufficient for administering therapeutic measures.

### **3. CLINICAL CONDITION**

It is not to be forgotten that this is an extraordinarily acute condition which does not compare to any other clinical condition and the classification given below is only of a didactic value. The physician should be very aggressive and should initiate treatment as soon as he deems it appropriate.

### CLINICAL STAGES IN FULMINANT MENINGOCOCCEMIA

EARLY PHASE FIRST 3 HOURS	TARDIVE PHASE AFTER 3 HOURS
1. Hyperpyrexia	1. Hyperpyrexia or hypothermia
2. Incipient purpuric exanthem	2. Extensive purpuric exanthem
3. Tachypnea	3. Mental Sopor and/or coma
4. Extremities are red and hot	4. Feeble pulse
5. Mental confusion	5. Pale and cold extremities
6. Myalgia, Arthralgia	6. Feeble pulse
7. Full pulse	7. Retarded capillary replenishment
8. Normal capillary replenishment	8. Hypotension and Tachycardia
9. Normal or Augmented Systemic Systolic Arterial Pressure	9. Narrow Pulse pressure
10. Wide Pulse Pressure	10. Ventilation diminished
11. Diminished systemic vascular resistance	11. Augmented central venous pressure
12. Adequate diuresis or polyuria	12. RVS augmented
13. Ventilation normal or augmented	13. Oligoanuria
	14. Paralytic Ileus

### FULMINANT MENINGOCOCCEMIA LABORATORY

EARLY PHASE FIRST 3 HOURS	TARDIVE PHASE II AFTER 3 HOURS
<ol style="list-style-type: none"> <li>1. Normal or hypoxaemia</li> <li>2. Narrow <math>O_2</math> arteriovenous difference</li> <li>3. Normal or increased <math>O_2</math> availability</li> <li>4. Respiratory alkalosis</li> <li>5. Hyperglycaemia</li> <li>6. Minimal alterations in coagulation</li> <li>7. Normal or slightly augmented lactacidemia</li> <li>8. Lactate/pyruvate relation normal or slightly augmented</li> <li>9. Slight Hyponatraemia and Hyperkalemia</li> <li>10. Urea, creatinine normal or slightly augmented</li> <li>11. The Haemogram does not provide any guidance</li> </ol>	<ol style="list-style-type: none"> <li>1. Hypoxaemia</li> <li>2. Wide <math>O_2</math> arteriovenous difference</li> <li>3. Diminished <math>O_2</math> availability</li> <li>4. Metabolic or mixed acidosis</li> <li>5. Hypoglycaemia</li> <li>6. DIC augmented</li> <li>7. Augmented lactacidemia</li> <li>8. Lactate/pyruvate relation clearly augmented</li> <li>9. Clear Hyponatraemia and Hyperkalemia</li> <li>10. Urea, creatinine clearly augmented.</li> </ol>

#### 4. TREATMENT

##### (A) DIET:

Will depend on the level of consciousness. In general it will be 0 with Gastrogastric Sound free fall.

##### (B) HYDRATION:

Its primary objective is to cover daily requirements, to which additional supplies to maintain an adequate capillary replenishment, a good diuresis, a good arterial pressure and central venous pressure should be added.

#### BASIC GUIDE FOR THE CALCULATION OF WATER AND ELECTROLYTE REQUIREMENTS

WEIGHT	GLUCOSE SOLUTION AT 10%
3 TO 10 KILOGRAMS	120 ML. PER KILO PER DAY
11 TO 20 KILOGRAMS	1000 ML. + 50 ML. PER EACH KILO OVER 10
+ THAN 20 KILOGRAMS	1500 ML. + 20 ML. PER EACH KILO OVER 20.

ELECTROLYTES	DAILY REQUIREMENTS
SODIUM	3 MEq. X KILO X DAY
POTASSIUM	2 MEq. X KILO X DAY

Sodium at 10% = 1 cc contributes with 1,7 MEq of Sodium  
Potassium at 10% = 1 cc contributes with 1,3 MEq of Potassium.

##### (C) ANTIBIOTICS:

- WITHOUT GERM CONFIRMATION: (IMMEDIATE, PRIOR TO BLOOD CULTURES)  
CEFTRIAXONE = ACANTEX = 100 Mgr. X KILO X DAY I.V. IN ONE DOSE OR  
CEFOTAXIME = CLAFORAN = 100 Mgr. X KILO X DAY I.V. EVERY SIX  
HOURS.

- CONFIRMED GERM (TARDIVE):

SODIUM PENICILLIN : 300.000 IU X KILO X DAY I.V. EVERY FOUR  
HOURS.

**(D) CORTICOIDS: (IMMEDIATELY, MEGADOSE)**

- BETAMETASONE=CIDOTEN → 2 Mgr. X KILO I.V. IN A SINGLE DOSE OR
- DEXAMETASONE=ORADAXON → 2 Mgr. X KILO I.V. IN A SINGLE DOSE OR
- METHYLPREDNISOLONE=SOLU-CORTEF → 40 MGR. X KILO I.V. IN A SINGLE DOSE
- HYDROCORTISONE → 150 Mgr. X KILO I.V. IN A SINGLE DOSE

If patient's condition stabilizes or does not worsen do not repeat.

**(E) OXYGEN THERAPY:**

Usual procedures to maintain a 100 mm Hg PaO<sub>2</sub>

**(F) DOPAMINE: (Improves cardiovascular condition)**

DOSE: 5-15 Mcg. X KILO X MINUTE

PRESENTATION: 5 ML ampules → 1 ML = 40 Mgr.

RECOMMENDED DILUTION: 6 X KILOGRAM OF WEIGHT = Dopamine Mgr. to be diluted in 100 ML. of glucose solution at 10%.

ADMINISTRATION OF DILUTION:

WITH INFUSION PUMP: 5 ML per hour is equivalent to 5 Mcg. per Kilo per Minute.

WITHOUT PUMP: 5 microdrops per minute is equivalent to 5 Mcg. per Kilo per Minute.

**(G) HYPOTENSION:**

- PHYSIOLOGIC OR LACTATED RINGER'S SOLUTIONS OR HAEMMACCEL OR PLASMA IN THE QUANTITY OF 20 ML. X KILO IN 10 MINUTES I.V. SHALL BE ADMINISTERED. THIS TREATMENT CAN BE REPEATED UNTIL THE PATIENT IS STABILIZED.

**(H) CONVULSIONS**

- DIAZEPAM: A dose of 0.3 - 0.5 Mgr per Kilogram of Weight, I.V. Can be repeated in 10 minutes.

**(I) ANALYSES**

- Haemogram, full + Sedimentation
- C-Reactive Protein
- Blood Cultures (2)
- Creatinaemia
- Urine, full
- Electrolytes in Plasma
- Arterial Astrup
- Glycaemia
- Lumbar Puncture
- Double Pharyngeal Smear

(J) Nursing

- Control of vital signs every 30 minutes or less, in accordance with seriousness of the patient's condition. A Guideline Table is attached, WHICH MUST BE SENT WITH THE PATIENT WHEN TRANSFERRED.
- Hydric Balance. Hourly measurement of diuresis.

GENERAL PRINCIPLES:

1. SHOCK DIAGNOSIS IS CLINICAL AND MUST BE MADE BEFORE IT BECOMES IRREVERSIBLE.
2. TREATMENT MUST BEGIN IMMEDIATELY.
3. THE PATIENT MUST BE TRANSFERRED WHEN HE/SHE IS STABILIZED.
4. THE ABOVE RELATES TO BASIC HANDLING OF SHOCK. FULL TREATMENT SHALL BE ADMINISTERED IN ANTOFAGASTA.

## THERAPEUTIC CRITERIA FOR SEPTIC SHOCK TREATMENT

Dr. Tomás Verdejo A.  
Dr. Antonio Cárdenas T.

### A. INITIAL GENERAL TREATMENT

1. BLOOD CULTURES (+)
2. HEMODYNAMIC STABILITY
3. BROAD SPECTRUM ANTIBIOTIC
4. MONITORING

### B. SPECIFIC TREATMENT

1. TREATMENT OF PRIMARY INFECTION
2. MYOCARDIUM FUNCTION
  - (A) IMPROVEMENT OF PRELOAD
  - (B) INOTROPIC AGENTS
  - (C) ↓ WORKING OF THE MYOCARDIUM
  - (D) CALCIUM INPUT
  - (E) REDUCING POSTLOAD
3. RESPIRATORY FUNCTION
  - (A) O<sub>2</sub>
  - (B) EARLY MECHANICAL VENTILATION
  - (C) PEEP
4. NORMALIZATION OF BIOCHEMICAL DISORDERS
  - (A) ELECTROLYTES
  - (B) GLUCOSE
  - (C) COAGULATION DISORDERS
5. CORTICOIDS
  - (A) EARLY ADMINISTERING
  - (B) METHYLPREDNISOLONE OR OTHER
6. USE OF TRANSFUSION WHITE BLOOD CELLS (NEUTROPHILS) (\*)
7. USE OF IMMUNOGLOBULIN (Ig). (\*) (\*)

(\*) ↑ NUMBER OF NEUTROPHILS USEFUL FOR THE DESTRUCTION OF PATHOGENIC AGENTS WHICH ARE BY THEMSELVES DIMINISHED THROUGH SEPTIC SHOCK.

(\*) (\*) PROVIDES ANTIBODIES THROUGH OPSONIZATION WHICH IS NECESSARY FOR THE DESTRUCTION OF THE PATHOGENIC AGENT.

Ig + BROAD SPECTRUM ANTIBIOTIC = DEMONSTRATED IMPROVEMENT OF MORTALITY IN SEPTIC SHOCK.

TABLE 1

GUIDELINES FOR PATIENTS SUFFERING  
FROM FULMINANT MENINGOCOCCEMIA

TIME								
TEMPERATURE								
HEART RATE								
RESPIRATORY FREQUENCY								
ARTERIAL PRESSURE								
DIURESIS								
CAPILLARY REPLENISHMENT								
COLOUR OF SKIN								
OXYGEN INSPIRATORY FRACTION 2								
GLASGOW SCALE								
PURPURIC LESIONS								

TABLE 2

## GUIDELINES FOR ADMINISTERED TREATMENTS

DATE/TIME	INDICATIONS
1.	
2.	
3.	
4.	
5.	
6.	
7.	
8.	

## **PUBLICATIONS**

CHILEAN SOCIETY OF PEDIATRICS  
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## C E R T I F I C A T E

CARLOS TORO A., Director - Editor of the  
Chilean Pediatrics Magazine hereby certifies that the research  
paper "Prognosis in Children with Meningococcal Disease"  
which author is ANTONIO CARDENAS T.  
has been approved by the Editorial Committee of the Magazine for  
publication in Volume 66, Nº 2, of 1995.

SANTIAGO, 21 April 1995

CTA/mal

CHILEAN SOCIETY OF PEDIATRICS

C E R T I F I C A T E

We hereby certify that the research paper entitled:

"Cefixime new alternative for meningococcus  
chemoprophylaxis"

Which authors are:

Cárdenas A., Contreras A., Rojas C.

Was presented at the XX CHILEAN PEDIATRICS CONVENTION,  
which took place in Concepción between 16 and 19 November, 1994

Dr. José Ignacio Infante L.  
Secretary-General  
Chilean Society of Pediatrics

Dr. Gustavo Solar V.  
President  
Chilean Society of Pediatrics

November, 1994

CHILEAN SOCIETY OF PEDIATRICS

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President  
Chilean Society of Pediatrics

November, 1994

## PROTOCOL

1. TITLE : Study of Neisseria Meningitidis carriers in the Pediatric Population of Antofagasta

2. INTRODUCTION :

The Meningococcal Disease has an endemic behaviour and reaches an incidence rate of 1-2 cases per 100.000 inhabitants.

A progressive increase in the incidence rate has been observed in Antofagasta, since 1987, which reached, last year, 17 cases per 100,000 inhabitants. The above situation has been a cause of concern to health authorities both at the regional and at the national levels.

One of the strategies to fight this disease, has been the search for an effective vaccine against Meningococcus Serogroup B which is responsible for the epidemic outbreak in our city. This has been done in conjunction with the United States Walter Reed Institute. Other measures that have been implemented at the regional level is the extension of the concept of exposure and the modification of the current national chemoprophylaxis regulations to increase adherence to them. In this same context we have considered it advisable to conduct a study of healthy carriers of Neisseria Meningitidis in what are considered to be the high-risk groups of the population in order to identify and treat them.

3. GENERAL OBJECTIVES:

To identify healthy carriers of Neisseria Meningitidis in the Antofagasta population aged between 0 and 18 years.

4. SPECIFIC OBJECTIVES:

- To determine the efficacy of Cefixime as a new chemoprophylaxis treatment.
- To know the distribution by age and sex of healthy carriers.
- To know socio-demographic aspects of healthy carriers.
- To create and maintain a data bank of healthy carriers.
- To identify risk factors of healthy carriers.

## 5. MATERIAL AND METHODOLOGY:

The size of the sample has been calculated using the Epi-Info Programme estimating a prevalence of healthy carriers of 10%, with 95% reliability and 1% of margin of error, in a universe of 84,000 children. This gave a sample of 1,000 children distributed by age, according to the weight percentage of each age group over the total infantile population.

The structuring of the sample will be made up through a selection of 5 pupils per class, using simple random sampling by drawing lots.

Data analysis will be conducted using the Epi-Info test 6.0 and SPSS, with a  $P < 0.05$  considered to be significant.

Two pharyngeal smears shall be taken from each pupil, using different swabs which shall be spread immediately onto Thayer-Martin (agar) medium plates.

The previously numbered and carefully closed plates will be deposited in an appropriate container in a humid environment (humid cotton wool) and with a CO<sub>2</sub> percentage of between 5 to 10% (lighted candle).

At the laboratory, the inoculum shall be dispersed over the rest of the plate, returned to its container in an appropriate environment, and left to incubate at 37°C for 48 hours.

Once this time has elapsed, any resulting suspect colonies will be subjected to the following determinations:

- a.- Gram stain
- b.- Oxidase test
- c.- Sugar fermentation test
- d.- Latex test
- e.- In vitro sensitivity to Cefixime

Once the *Neisseria Meningitidis* colonies are identified they will be sent via the normal channels to the Public Health Institute in Santiago for confirmation and serotyping.

In accordance with our capability, it is planned to take one school per day as the duration of this study is of two weeks as of 17/04/95.

In those cases that turn out to be positive for *Neisseria Meningitidis*, a computer record sheet will be opened as per the attached sample. Persons with a positive smear for *Neisseria Meningitidis* will be administered 400 mgs. of Cefixime for two days in the case of adults and 8 mg/kg in syrup form for two days in the case of children.

Each pupil shall fill in an epidemiology survey which has been previously validated by the Panamerican Health Organization in Santiago.

**6.- STAFF:**

a.-	Dr. Antonio Cárdenas T.	Physician
b.-	Ms. Andrea Contreras G.	Nurse
c.-	Mr. Claudio Rojas	Medical Technician
d.-	Ms. Rosa Rivera A.	Secretary

**7.- DURATION:**

Starting date	:	17 April 1995
Completion date	:	28 April 1995

## PROTOCOL

1.- TITLE : Study of Neisseria Meningitidis carriers, Public School D-65, Antofagasta.

2.- INTRODUCTION :

Meningococcal Disease is endemic and its incidence rate is 1-2 cases per 100,000 inhabitants.

This incidence rate, however, has been increasing progressively in Antofagasta since 1987, and last year 17 cases per 100,000 inhabitants were recorded. This situation has caused concern among health authorities both at a national and regional level.

One of the strategies to combat this disease is to try to develop a vaccine that would be effective against Meningococcus serogroup B, which is responsible for the outbreak in our city, and work in this direction is currently being carried out in conjunction with the U.S. Walter Reed Institute. Other measures we have implemented at a regional level are to broaden the concept of contact and modify the current national norms on chemotherapy with an aim to increase adherence to those norms. In this same context, we have considered it advisable to conduct a study of healthy carriers of Neisseria Meningitidis in what are considered to be high risk groups of the population, in order to identify and treat both them and their contacts.

3.- GENERAL OBJECTIVE:

To identify healthy Neisseria Meningitidis carriers in a public primary school.

4.- SPECIFIC OBJECTIVES:

- To identify Neisseria Meningitidis carriers among the contacts of healthy carriers at the school.
- To determine the effectiveness of Cefixime as a new treatment in chemotherapy.
- To establish the distribution by age and sex of healthy carriers.
- To establish the epidemiological aspects of healthy carriers.
- To start up and maintain a data base of healthy carriers.

## 5.- MATERIAL AND METHOD:

The size of the sample was calculated using the EPI-INFO programme, estimating a prevalence of healthy carriers of 15%, with 95% reliability and 5% margin of error, in a universe of 1,348 enrolled students. This gave us a sample of 180 children, who were stratified according to the percentage of each level of schooling in the total student population:

Level	Number	Percentage
Pre-school	23	12.6%
Basic Cycle I	83	46%
Basic Cycle II	74	41%
T O T A L	180	100%

The sample will be made up of five students per class, using simple random sampling by drawing lots.

The statistical analysis will be conducted using the Chi squared test, with a  $p < 0.05$  level considered to be significant.

Two pharyngeal smear samples will be taken per student, using different swabs, and will be implanted immediately on Thayer Martin agar slides.

The previously numbered and carefully closed slides will be deposited in an appropriate container in a humid environment (humid cotton wool) and with a percentage of  $CO_2$  of 5 to 10% (lighted candle).

Once at the laboratory, the inoculum will be dispersed over the rest of the slide, returned to its container in an appropriate environment, and left to incubate at  $37^\circ C$  for 48 hours.

Once this time has elapsed, any resulting suspect colonies will be subjected to the following determinations:

- a.- Gram stain
- b.- Oxidase test
- c.- Sugar fermentation test
- d.- Latex test
- e.- In vitro sensitivity to Cefixime

Once the *Neisseria Meningitidis* colonies are identified they will be sent via the normal channels to the Public Health Institute in Santiago for confirmation and serotyping.

Our plan is to take a maximum of ten samples per day for processing.

For cases that turn out to be positive for Neisseria Meningitidis, a computer record sheet will be opened up as per the attached sample. Persons with a positive smear for Neisseria Meningitidis will be administered 400 mgs. of Cefixime for two days in the case of adults and 8 mg/kg in syrup form for two days in the case of children.

The smear test will be repeated seven days later in order to verify whether the Neisseria Meningitidis has been eradicated. Chemotherapy will be understood to be successful if the smear test of the 7th. day is negative and unsuccessful if it is positive.

Chemotherapy will be administered in the presence of one of the researchers.

Two weeks (14 days) after the first smear was taken, another control smear will be taken to check whether any recolonization has taken place.

In all cases where Cefixime has failed the chemotherapy currently in use will be administered.

Pregnant women will be excluded from this study.

#### 6.- STAFF:

a.- Dr. Antonio Cárdenas T.	Physician
b.- Ms. Andrea Contreras G.	Nurse
c.- Mr. Claudio Rojas	Medical Technologist
d.- Ms. Rosa Rivera A.	Secretary

#### 7.- DURATION:

Starting date : 02 May 1994  
End date : 15 June 1994

1.- TITLE:

CEFIXIME: NEW ALTERNATIVE FOR MENINGOCOCCAL CHEMOTHERAPY

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4.- FUNDING:

STUDY FINANCED BY THE WALTER REED ARMY INSTITUTE RESEARCH  
AND PAHO/WHO IN CHILE.

**TITLE:**

**CEFIXIME: A NEW ALTERNATIVE FOR MENINGOCOCCAL CHEMOTHERAPY**

**ABSTRACT:**

At a public primary school located in a sector of Antofagasta with a high incidence of meningococcal disease, a random sample of 216 children between the ages of 5 and 14 was taken, of which eighteen (8.3%) proved to be carriers of *N. Meningitidis* group B.

In order to test the effectiveness of Cefixime to eradicate *N. Meningitidis* in healthy carriers, Cefixime in suspension was administered in a single dose of 8 mg/kg. per day for two days. 72.2% (13/18) had no adverse reactions whatever and 27.8% (5/18) had mild reactions that disappeared spontaneously. No pharyngeal culture was positive after 7 and 14 days, nor after three months following treatment. In spite of the limitations of our study, we believe Cefixime to be an effective alternative in meningococcal chemotherapy.

## 2.- INTRODUCTION:

Chemotherapy using antibiotics is widely recommended in the contact of patients with meningococcal disease, with Rifampin as the preferred drug (1, 2). Its use, however, has several major drawbacks, among them adverse effects (3, 4) such as headache, vertigo and gastrointestinal discomfort in 25% of cases; treatment failure in 20% of cases (5); it is teratogenic in animals and contraindicated in pregnancy. In addition, Rifampin-resistant strains have been detected and documented. The four-dose regimen associated with the frequency of adverse reactions diminishes adherence to treatment. In adults, a single oral dose of Ciprofloxacin (7) and Ceftriaxone (8, 9) have proved to be valuable alternatives. Cefixime, a third generation orally active cephalosporin, has shown a strong inhibiting effect against *N. Meningitidis* in vitro (10, 11, 12). The purpose of our study was to determine the effectiveness of Cefixime in the erradication of *N. Meningitidis* in healthy carriers.

### 3.- MATERIAL AND METHOD:

A sample of 216 children between the ages of 5 and 14 was taken at a public primary school with an enrollment of 1,384 students, located in a sector of Antofagasta where there is a high incidence of meningococcal disease. The sample was stratified according to the percentage of each level of schooling in the total student population. The sample was made up of five students per class, using simple random sampling. Two pharyngeal smear samples were taken per student, using different swabs, and implanted immediately on Thayer Martin agar slides. These were deposited in an appropriate container in a humid environment (humid cotton wool) with a percentage of CO<sub>2</sub> of 5 to 10% (lighted candle), after which they were incubated at 37°C for 48 hours. The suspect colonies were subjected to the following determinations: Gram stain, cytochrome oxidase test, QuadFer<sup>®</sup> sugar fermentation test and latex test. Children with a positive culture for *N. Meningitidis* were administered Cefixime in suspension in a single dose of 8 mg. per kg. of weight per day (0.5 ml. per kg. of weight per day) for two days, in the presence of one of the research team. Control smears were taken 7 days, 14 days and 3 months after treatment. The size of the sample was calculated using the EpiInfo programme, with an a priori estimate of 15% carrier prevalence. The statistical analysis was conducted using the Chi squared test, with a  $p < 0.05$  level considered to be significant.

#### 4.- RESULTS:

Eighteen N. Meningitidis group B carriers were identified, making up a carrier state of 8.3% (18/216). All control smears at 7 and 14 days after treatment, as well as those taken three months later, were negative. No statistically significant differences were found in the distribution by sex; by age, however, 49.9% (9/18) of the carriers were in the 11-14 age range (Table No 1). 72% (13/18) did not report any discomfort up to 48 hours after the medication was administered (Table No 2), 22.2% (4/18) reported headache, 11.1% (2/18) reported feverishness, 5.5% (1/18) diarrhoea and 5.5% (1/18) abdominal pain, all of them mild discomforts that disappeared spontaneously.

## 5.- DISCUSSION

The 8.3% carrier state ratio for *N. Meningitidis* group B obtained at the primary school was similar to that reported in previous studies conducted in Arica in 1989 (8.2%) and Iquique in 1987 (11.5%) for the general population, with a total of 3,038 samples (unpublished observations by Dr. W. Zollinger). Similar results were found in another study conducted in Zagreb (11). It is necessary, however, to bear in mind that the age distribution of the samples of each study was different, which limits the possibility of making comparative analyses.

According to other large studies (12, 13), Cefixime has proved to be a safe drug, its main adverse reaction being mild gastrointestinal discomfort which did not require suspending treatment. Adverse reactions were reported in a range of 1.4% to 38%, similar to those we encountered in our experience (11.1%), which were also mild reactions that disappeared spontaneously. In general, the medication in suspension form proved to be very well tolerated, in addition to its convenient two-dose administration; in contrast, Rifampin is not easily obtainable in the form of suspension in our media, so that it is necessary to resort to preparing slips of paper containing the dose, which is difficult to administer to unweaned infants.

No pharyngeal culture was positive after 7 and 14 days, nor has any recolonization taken place after three months following treatment.

In spite of the limitations of our clinical experience,  
we believe Cefixime to be a safe and effective alternative  
for meningococcal chemotherapy in children.

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1.- TITLE:

PROGNOSTIC FACTORS OF MENINGOCOCCAL DISEASE IN CHILDREN

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4.- FUNDING:

STUDY FINANCED BY THE WALTER REED ARMY INSTITUTE RESEARCH  
AND PAHO/WHO IN CHILE.

**TITLE:**

**PROGNOSTIC FACTORS OF MENINGOCOCCAL DISEASE IN CHILDREN**

**ABSTRACT:**

From 1 January 1987 to 31 December 1992, retrospectively, and 1 January 1993 to 31 July 1994, prospectively, we collected clinical and laboratory data of 67 children in Antofagasta who had suffered meningococcal disease. The purpose was to evaluate the Stiemh and Damrosch score and other factors as predictors of the evolution of this disease on admission.

We found that each of the factors: purpura of less than 12 hours' evolution prior to admission; presence of shock; absence of meningitis; white corpuscles  $< 10,000$  and erythro sedimentation rate (E.S.R.)  $< 10$  were associated with a higher risk of death. The same was observed in the case of purpura fulminans and impaired level of consciousness. When we applied the Stiemh and Damrosch score, we found that when it added up to three or more points the mortality rate was over 75%, which indicates that it continues to have a very good predictive value. We suggest conducting further prospective and multivariate analysis studies in order to gain insight into the interaction between individually studied factors.

## 2.- INTRODUCTION:

Meningococcal disease continues to be a major cause of morbidity and mortality in children (1, 2). Our country has not been an exception to this reality and in 1979 there was an epidemic outbreak of meningococcal disease serogroup B in Iquique (3, 4) which then spread to Antofagasta, reaching its maximum incidence of 17 cases per 100,000 inhabitants in 1992 (unpublished observations).

There is probably no other disease in Pediatrics that is capable of killing a child within a few hours. This explains the interest of and challenge to clinicians to have available at the time of admission an evaluation system that would allow them to rapidly identify those patients with an unfavourable prognosis in order to subject them to more aggressive treatments. Of late, several researchers (5, 6, 7, 8, 9, 10) have tried to provide an answer to this concern, but using designs that differ in terms of sample size, definitions and statistical methods. Among these research studies, factors that have been associated with an unfavourable prognosis are: white corpuscle count  $< 10,000$  or  $< 5,000$  on admission; presence of shock on admission; impaired level of consciousness (stupor or coma) on admission; platelet count  $< 100,000$ ; purpura fulminans; absence of meningitis; erythro sedimentation rate (E.S.R.)  $< 10$  on admission; exanthema with less than 12 hours' evolution prior to admission; hypothermia; hyperpyrexia; excess base; glycemia. Of these, there is greater consensus regarding the first five factors.

In 1966, on the basis of 63 cases, Stieh~~n~~ and Damrosch (11) identified five factors present on admission that were associated with an unfavourable prognosis: purpura of less than 12 hours' evolution prior to admission; presence of shock (systolic pressure  $< 70$ ); absence of meningitis; white corpuscle count in peripheral blood  $\leq 10,000$  and E.S.R.  $\leq 10$ . One point was assigned to each factor and a score of 3 or more was associated with a mortality rate of over 85% (12). Using these and other variables, Niklasson published similar results in 1971 (13). Because of the simplicity of the score and its ready availability to all clinicians, we wanted to verify its current validity, as well as that of other factors, using our recent epidemic outbreak as a basis for this experience.

### 3.- PATIENTS AND METHOD:

Between 1 January 1987 and December 1992, retrospectively, and from 1 January 1993 to 31 July 1994, prospectively, clinical and laboratory data of 67 children between the ages of 0 and 15 in the city of Antofagasta with a diagnosis of meningococcal disease upon discharge were collected and recorded in a computer data base.

Confirmation of the presence of *N. Meningitidis* was established by one or more of the following criteria: isolation of *N. Meningitidis* in cephalorachidean liquid (C.R.L.) or blood, C.R.L. Gram stain, C.R.L. latex test, and necropsy when the clinical condition was categorical for meningococcal disease but the above tests were all negative. 80.5% (54/67) of the cases were diagnosed by positive C.R.L. or blood cultures, 11.9% (8/67) by C.R.L. Gram stain, 4.47% (3/67) by necropsy and 2.98% (2/67) by the latex test.

The same definitions as those used by Stiemh and Damrosch were applied:

Meningitis: Positive C.R.L. culture with more than 20 white corpuscles per c.c.

Meningococemia: Purpuric syndrome with positive blood cultures.

Shock: systolic pressure equal to or less than 70 mm. of Hg.

We were also interested in studying the presence of purpura fulminans, which was defined as the presence of purpuric exanthema associated with shock (systolic pressure < 70), and impaired level of consciousness, which was defined as the presence of stupor or coma.

All these factors were evaluated on admitting the patient and a determination was made regarding whether or not they were associated with the risk of death. The Stiehle and Damrosch Score was subsequently applied to each patient and the score obtained was related to the patient's condition upon discharge.

The statistical analysis of the differences in evolution of each factor was made using the Epi-Info programme and the Chi squared and exact Fisher tests. Unless indicated otherwise, a  $p < 0.05$  was considered significant.

#### 4.- RESULTS:

Eight patients (four boys and four girls) died, making up an overall mortality rate of 11.9% (8/67). A higher mortality rate, reaching 33% (4/12), was observed in children under 12 months. According to the age/weight ratio (NCHS/WHO table), 73% (49/67) of the patients were eutrophic. No statistically significant differences were found either with regard to the distribution by sex or by seasons of the year.

According to the clinical presentation, 70.1% (47/67) of the cases were solely meningitis, 16.4% (11/67) were solely meningococemia, and 13.4% (9/67) were mixed. Of the patients who died, seven had meningococemia on its own and one had a mixed condition. No patients affected solely by meningitis died (see Table No 1), and it was found that the absence of meningitis was associated with the risk of death ( $p = 0.0000029$ ). Seven out of nine patients who were in shock on admission died, and this factor was also associated with the risk of death ( $p = 0.0000003$ ). An E.S.R.  $< 10$  on admission was found in nine patients, of whom four died (Table No 2), and was also associated with the risk of death ( $p = 0.00029$ ). In terms of a white corpuscle count of less than 10,000 on admission, this was found in thirteen patients, of whom seven died (Table No 3), and was associated with the risk of death ( $p = 0.00002$ ). Finally, out of thirty patients who presented exanthema with less than 12 hours' evolution prior to admission, eight died, and

this was also associated with the risk of death ( $p = 0.0129$ ). The presence of purpuric exanthema on admission, however, regardless of the period of evolution, was not associated with the risk of death ( $p = 0.09$ ), in contrast with purpura fulminans, where eight out of ten patients admitted with this diagnosis died ( $p = 0.000075$ ). The same was true for impaired level of consciousness, where seven out of nine patients presenting stupor or coma died ( $p = 0.0000003$ ).

On applying the Stienh and Damrosch score, we found that when the score was equal to or higher than 3, the mortality rate increased sharply (Table Nº 4). This was also the case when the patients of both experiences were grouped together (Table Nº 5).

## 5.- DISCUSSION:

We examined each of the Stiehm and Damrosch factors in relation to the risk of death, in order to reproduce this experience in our patients. We found that each factor was associated with the risk of death, in contrast with the results of other authors (5, 6) who did not find any relationship between the absence of meningitis and the time of evolution of exanthema with the risk of death. These same researchers and others (7, 8, 10) coincide, however, in that the presence of shock and a low white corpuscle count on admission are still good predictors. An E.S.R. of  $< 10$  has not been studied again, but we found that it was related to an unfavourable evolution of the disease. As in the cited references, we also found that purpura fulminans and impaired level of consciousness were highly associated with the risk of death. Because of lack of information we were unable to evaluate thrombocytopenia.

We found that the Stiehm and Damrosch score still appears to be a good predictor of the outcome of the disease, contrary to Tesoro (5) who believes it is only effective in identifying patients who will have a favourable evolution.

It is our belief that this score, because of its simplicity and ready accessibility to every clinician, should be used to identify the most critical patients, for whom we advocate an aggressive treatment from the outset on

the basis of early mechanical ventilation, high doses of corticosteroids, vasoactive drugs and an adequate use of volume to prevent the cold phase of septic shock.

We believe, finally, that the limitation of our study due to its mainly retrospective nature, makes it absolutely necessary to propose future prospective and multivariate analysis studies which would give us greater insight into the interactions between factors that have up to now only been studied individually.

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## REFERENCES:

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Scand. J. Infect. Dis. 1971, 3: 17-25.

1.- TITLE:

ACUTE BACTERIAL MENINGITIS IN CHILDREN OF ANTOFAGASTA:  
FIVE-YEAR EXPERIENCE

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### 1.- TITLE:

ACUTE BACTERIAL MENINGITIS IN CHILDREN OF ANTOFAGASTA:  
FIVE-YEAR EXPERIENCE

### 2.- INTRODUCTION:

The availability of new and effective antibiotics, together with support measures, have notably improved the prognosis of acute bacterial meningitis (A.B.M.) in children (1).

It is, however, a diagnosis that continues to present challenges to physicians due to its high mortality rate and sequelae. (2)

The purpose of this study is to establish some clinical and epidemiological aspects of A.B.M. in children of Antofagasta.

### 3.- MATERIAL AND METHOD:

Our study encompasses a total of 137 children, excluding newly-borns, who were diagnosed with A.B.M. during the period between 1 January 1989 and 31 December 1993 in Antofagasta. An instrument was designed, which was previously validated and where the data from the retroactively gathered medical records were recorded.

A.B.M. was defined as the condition of persons presenting compatible cytochemical cephalorachidian liquid (C.R.L.) alterations (2). The etiology was assigned according to positive results in one or more of the following tests: C.R.L. culture, blood culture, C.R.L. latex

test or C.R.L. Gram stain. If they were all negative, the disease was attributed to an unknown agent. The statistical analysis was carried out using the Chi squared test, with a  $p < 0.05$  considered to be significant.

#### 4.- RESULTS:

According to the case histories of our study, the most frequent etiological agents were *N. Meningitidis* (46%), *H. Influenzae* (18%) and *S. Pneumoniae* (8.8%), with no specific cause established in nearly one-third (27%) of the cases (Table Nº 1). In the period under study the annual incidence rate was 38.4 cases per 100,000 children on average, with the highest incidence found in children under 24 months of age (Table Nº 2); the mortality rates were also highest in that age bracket (Table Nº 3). Of the deceased patients, six died of *S. Pneumoniae*, five of *N. Meningitidis*, one of *H. Influenzae* and one due to an unknown agent. 62.75% were eutrophic and 18.2% were overweight. No statistically significant differences were found either in the distribution by sex or by season. 62.7% of the cases consulted within the first 24 hours and 85.4% did so within 72 hours after the symptoms first appeared (Table Nº 4). Fever was present in 99.3% of cases, followed by vomiting in 62.7%. Meningeal signs were present in only 54% (Table Nº 5). The C.R.L. cultures (n=137) were positive in 54% of the cases. The blood cultures recorded (n=67) were positive in 16.6% of cases and the latex tests (n=39) were positive in

27% of cases. 72% of the patients were hospitalized between 7 and 15 days, at an average of 11 days (Table Nº 6). 85.4% were discharged alive and apparently without any sequelae, 5.1% had evident sequelae and 9.5% died.

## 5.- DISCUSSION:

In contrast with other national (2, 3, 4) and foreign (5, 6) experiences, the main etiological agent found in our study was *N. Meningitidis* (47.8%), followed by *H. Influenzae* (18%) and *S. Pneumoniae* (8.8%). This is explained by an epidemic outbreak of meningococcal disease that has been affecting our city since 1987, and that during 1992 reached an annual incidence rate of 17 cases per 100,000 inhabitants, vis-à-vis a rate of 1-2 cases per 100,000 inhabitants in normal times. This also explains the high annual incidence rate of acute bacterial meningitis (A.B.M.), which in 1991 reached 50.7 cases per 100,000 children, a considerably higher figure than that recorded in the literature (7, 8). In our study, the age group with the highest risk of getting infected, evaluated by the incidence rates, were children under 24 months, which coincides with the findings of other publications (9, 10, 11). The same occurs with the risk of death, where the mortality rate of children under 24 months, who concentrate 75% of the death rate, is 3.8 times greater than the combined rate of all other age groups. The first causal agent of death in our series was *S. Pneumoniae*, similar to the findings of other

studies (12, 13). Our patients consulted quite early in comparison with other experiences (10, 17), as 62.7% of the cases were admitted within the first 24 hours of the appearance of symptoms. This is explained by the heightened sensitivity there is in the community with regard to this problem as a result of extensive educational campaigns developed by the local health agencies. This has also resulted in our having a mortality rate (9.5%) similar to that recorded in foreign publications (14), but lower than the national average (10, 15, 16, 17). Fever was present in 99.3% of cases, followed by vomiting in 62.7%. Meningeal signs were found in only 54% of cases, which confirms a frequent lack of specificity in the clinical presentation, thus forcing the physician to diagnose on the basis of high suspicion and, in the face of the slightest doubt, perform a lumbar puncture. The discriminatory performance of our laboratory tests was low in comparison with other experiences (18, 19), which tends to explain our 27% of meningitis attributed to unknown agents. 85.4% were discharged alive and apparently with no sequelae, although no specialized follow-up studies were carried out. These results are satisfactory, but would merit longer-term studies.

## 6.- ABSTRACT:

A retrospective study was made of 137 cases of acute bacterial meningitis in children of Antofagasta recorded between 1 January 1989 and 31 December 1993. The most frequent etiological agents were *N. Meningitidis*, *H. Influenzae* and *S. Pneumoniae*, accounting for 46%, 25% and 12% respectively. These results are explained by an epidemic outbreak of meningococcal disease during the period under study. In 27% of cases the agent was unknown. No statistically significant differences were found in the distributions by sex or season. Children under 24 months of age had the highest risk of becoming infected by and dying of acute bacterial meningitis. 62.7% were hospitalized within the first 24 hours of the appearance of symptoms. Fever, vomiting and meningeal signs were present in 99.3%, 62.7% and 54% of cases, respectively. The results of cephalorachidian liquid (C.R.L.) cultures, blood cultures, C.R.L. latex cultures and Gram stains were 54%, 16.6%, 27.2% and 48.1% respectively. The mortality rate was 9.5%.

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## **PRESS ARTICLES**

**Pequeña paciente al borde de la muerte en el Hospital de Antofagasta**

# A 29 subbieron los casos de meningitis

Página 28

## Salud detectó otro caso de meningitis

A 29 se eleva el número de casos de meningitis en la región, luego de confirmarse ayer la enfermedad en una menor proveniente de Tocopilla, la cual se encuentra en grave estado de salud y en tratamiento en el Hospital Regional de Antofagasta. Este nuevo caso, corresponde a la meningitis meningocócica tipo B.

La menor de sólo 5 me-

ses de edad, fue derivada del Hospital "Marcos Maquada" del vecino puerto, al Hospital Regional de Antofagasta, donde se indicó que según el diagnóstico médico, se encuentra en grave estado de salud debido a una meningococcemia.

La información emanó del Secretario Regional Ministerial de Salud, doctor

Mario Besnier Hernández, quien señaló que con este caso la cifra en Tocopilla se eleva a tres y la regional a 29.

Por su parte el doctor Antonio Cárdenas Tadiach, encargado del laboratorio de Vigilancia Permanente de Enfermedades Meningocócicas del Servicio de Salud, manifestó que la menor pro-

viene del pasaje Esmeralda del vecino puerto.

Según antecedentes provenientes de allí, éste se encuentra en el sector norte alto de la ciudad y pertenece a un populoso barrio con viviendas modestas.

Asimismo el facultativo señaló que la menor fue internada el martes y ayer a primera hora se determinó su traslado a la capital re-

gional, en un denodado esfuerzo médico por salvarle la vida. Sin embargo, su situación hasta anoche era en extremo delicada y se esperaba un desenlace fatal en cualquier momento.

Pese a ello el equipo médico que la atiende, realizaba gran esfuerzo para revertir la situación y salvarle la vida, pero según manifestó

el doctor Cárdenas, la niña se encuentra muy grave.

Una vez más tanto el Seremi Besnier, como el médico encargado del laboratorio insistieron en la consulta precoz, aunque coincidieron en que una meningococcemia es en extremo delicada, por cuanto el bicho se va a la sangre y produce un ataque generalizado.

**Empeoró cuadro de lactante internado en hospital antofagastino**

# Situación crítica por una meningitis

EL MERCURIO, Miércoles 18 de agosto de 1993

## En estado crítico lactante afectada por meningococcemia

Una lactante de 7 meses se debate entre la vida y la muerte, afectada de una meningococcemia.

La niña ingresó al Hospital Regional atacada un cuadro respiratorio, sin embargo hizo la enfermedad mientras era asistida, lo que significa, según el diagnóstico médico que estaba en incubación.

De acuerdo a la información proporcionada por el doctor Alex Arroyo Meneses, subdirector Médico del Servicio de Salud, la sintomatología presentada por la menor cuando fue internada, no hacia presagiar que deriva-

ra en una meningococcemia, patología de la meningitis meningocócica tipo B, que es la más delicada por cuanto la infección se va a la sangre.

El facultativo indicó que la guagua se encuentra en estado grave y está conectada a un respirador, mientras se le practica el tratamiento adecuado a fin de sacarla de su estado crítico.

Sin embargo, dijo, la meningococcemia es uno de las fases de mayor gravedad que presenta la meningitis meningocócica.

Las autoridades de Salud indicó que la menor tiene su domicilio en el sector norte

de la ciudad y que su cuadro se presentó luego de cinco semanas sin haberse producido un caso de meningitis.

Reiteró las recomendaciones para tratar a tiempo la enfermedad y fue enfático al señalar que en ningún caso se está frente a una epidemia. Dijo estar de acuerdo con los planteamientos del doctor Tomás Verdejo Aguirre, presidente del Consejo Regional del Colegio Médico y recordó que el Servicio de Salud de Antofagasta, hizo una campaña intensiva en 1991, la que será re-

forzada actualmente por la comisión mixta de vigilancia de la enfermedad.

Viernes 16 de julio de 1993

La Estrella del Norte

Nueva estrategia para combatir el mal

# MENINGITIS: BUSCARAN A PORTADORES DEL GERMEN



En primer plano, los especialistas norteamericanos Kischner y Zollinger, a la derecha el Jefe de Epidemiología del Ministerio de Salud, doctor Jorge Toro.

## Buscarán a portadores de meningitis en Antofagasta

La implementación de un programa para la búsqueda de portadores en Antofagasta, es una de las iniciativas de Salud para combatir el brote epidémico de meningitis en la capital regional. Así lo dio a conocer el doctor Jorge Toro, Jefe de Epidemiología del Ministerio de Salud, quien visitó nuestra ciudad.

Consultado por este diario, la alta autoridad de salud señaló que "en el ámbito de la preocupación existente a nivel ministerial por la meningitis en Antofagasta, hay propuestas de poder hacer estudio de portadores".

"Normalmente en una población existen portadores de meningococos y por alguna razón que se desconoce, se produce mayor incremento de portaciones en las personas y se producen estos brotes epidémicos. No se sabe que es lo que gatilla este incremento en determinado momento", explicó el doctor Toro.

"Como existe esta preocupación muy grande, la idea es hacer estudios en algunos grupo de población. También se está buscando más información científica para poder ir controlándolo, ya que el problema de la meningitis lo tenemos muy presente".

Consultado acerca del financiamiento que reciben estos estudios de alto costo, el epidemiólogo respondió, "efectivamente son de alto costo y la gran mayoría está siendo soportado financieramente por el hospital norteamericano "Walter Reed", existiendo también un aporte del Servicio de Salud. Hay interés por ambas partes de mantener esta colaboración".

Con respecto al nivel en que se encuentra el proyecto, el doctor Toro señaló "el equipo local está en estos momentos haciendo la propuesta. Se está viendo todo el protocolo con bastante fineza para hacer este estudio en el que en principio estarían de acuerdo lo investigadores del Walter Reed".

Miércoles 21 de julio de 1993

**Autoridad de Salud se refirió al problema de la meningitis**

# No existe compromiso con vacuna norteamericana

La inexistencia de un compromiso formal que "amarre" al Ministerio de Salud chileno para aplicar la vacuna norteamericana que se está desarrollando en parte en Antofagasta, fue dada a conocer por el Jefe de Epidemiología de esa entidad, doctor Jorge Toro.

Señaló la autoridad que dicha disposición había sido ratificada por los dos expertos norteamericanos que trabajan en la vacuna y lo acompañaron, en la visita que efectuó a esta capital regional.

"Los norteamericanos se han entrevistado con autoridades del Ministerio, dejando abierta la posibilidad de otras vacunas. Este proyecto no amarra necesariamente al país frente a la posibilidad

de que se obtenga el día de mañana progreso en otros lugares con otras vacunas. Esto no compromete ninguna decisión ministerial con este proyecto. Son cosas absolutamente distintas", dijo el doctor Toro.

Con respecto al avance de esta vacuna, señaló: "por el momento habría una postergación de lo que habíamos previsto, hasta no proveer de una vacuna que no va a producir reacciones. Aunque esa parte está superada, lo que nosotros y el equipo del doctor Walter Reed buscamos es una vacuna que realmente proteja, de protección y respuesta inmunológica segura".

Consultado sobre las acciones que realizan las auto-

ridades ante la posibilidad de un brote epidémico de meningitis en Antofagasta, respondió que "hay una preocupación muy grande del Ministro, del subsecretario, de otras autoridades ministeriales y del Servicio de Salud. Se ha conformado un comité regional. Estamos haciendo un seguimiento muy fino de la tendencia, no sólo

aquí en la Segunda Región, en otras zonas del país y se busca una respuesta y solución a esto".

Acerca de la forma en que se trabaja en otras partes del mundo contra este flagelo, el doctor Toro señaló: "hay en proceso una vacuna canadiense. Hay muchos grupos trabajando en diferentes países, en Noruega,

en Cuba, en Brasil, en Holanda. Buscan un producto inmunológico muy seguro para la población y una buena respuesta en la gente. Se está trabajando en Francia en el desarrollo de una vacuna con cápsulas y con polisacáridos, que son partes que componen el meningococo". Consultado acerca del resultado que han obtenido los norteamericanos en otras partes del mundo, los mismos especialistas estadounidenses Kischner y Zollinger respondieron que "el Hospital Walter Reed previamente ha trabajado, hace años atrás, con Noruega y algunos trabajos de colaboración con Brasil, sin embargo hoy día el trabajo es exclusivo con Chile".

DOCTOR ANTONIO CARDENAS T.

## Meningitis Meningocócica

La Meningitis Meningocócica a pesar de los grandes avances tecnológicos continúa siendo un importante problema de Salud Pública que se ha traducido en brotes epidémicos en diferentes áreas del mundo. El lugar más afectado es el llamado el Cinturón de la Meningitis ubicado en el África y que se extiende desde el Sudán por el Este hasta Mali en el Oeste.

Durante el período comprendido entre 1951 y 1960 hubieron por lo menos 340.000 casos que resultaron en 53.000 muertes.

Desde la Segunda Guerra Mundial, la Organización Mundial de la Salud ha calculado una Tasa de Incidencia Anual de 70 casos por 100.000 habitantes en esa región. Aunque en menor grado, esta situación se viene repitiendo en los diferentes continentes.

Esta enfermedad es característica de los niños más pequeños, sin embargo, en algunas poblaciones que son cerradas el riesgo de enfermar es sustancialmente mayor incluyendo a los adultos. Es el caso por ejemplo que se presenta en las grandes movilizaciones militares. Investigaciones que se iniciaron en los años 60, en el Instituto Walter Reed de los Estados Unidos condujeron al desarrollo de una vacuna purificada contra el Meningococo Grupo C.

Su uso rutinario en los conscriptos norteamericanos se inició el año 1971 y se tradujo en una dramática disminución de la enfermedad provocada por este germen. En el año 1979 se fabrica una vacuna bivalente que nos permite ahora combatir Meningococo A y C la cual ha sido administrada a millones de seres humanos en el mundo incluyendo a Chile. Los éxitos continúan y es así como en el año 1982 se agregan los componentes necesarios para combatir a los Meningococos W135 e Y.

Nace así una vacuna tetravalente que actualmente es usada en forma rutinaria

en todos los conscriptos que ingresan a hacer su Servicio Militar en los Estados Unidos.

El Meningococo Grupo B, es el responsable del 50% de las Meningitis Meningocócica de los Estados Unidos hoy día y en Chile sobre el 97%. En Antofagasta e Iquique es la única causa y éste fenómeno se está reproduciendo en prácticamente todos los Servicios de Salud del país. En otros lugares como Noruega, Sudáfrica, Inglaterra, Brasil y Cuba también se han visto afectados por el mismo problema en los años recientes.

Hoy día, no existe una vacuna disponible, que sea efectiva contra éste germen. De allí el interés, y el esfuerzo que realizan grupos de científicos de diferentes partes del mundo para solucionar este problema. Cuba, un pequeño país latinoamericano, no se ha quedado atrás y disponen y comercializan actualmente una vacuna. Sin embargo, se mantienen serias dudas sobre su eficacia razón por la que no se ha autorizado su uso en el país, lo que no ha impedido que un grupo de científicos chilenos la estén constantemente evaluando.

La reciente visita de los médicos norteamericanos del Instituto Walter Reed con quienes tenemos un Proyecto de Investigación en conjunto, fue para, entre otras cosas, anunciar que la actual línea de trabajo no produjo los resultados esperados. Dicho de otra forma la vacuna fabricada no fue mejor que las disponibles actualmente y no será usado en los plazos previstos.

Esto mismo avala la honestidad y seriedad con que se está procediendo en ésta materia. Es importante también destacar que el actual trabajo, no impide en absoluto, que si otras investigaciones descubren o fabrican una vacuna que nos de seguridad de su calidad, será inmediatamente aplicada a la población.

# ¿Qué pasa en Antofagasta con la meningitis?

## "SI. TENEMOS UN BROTE EPIDÉMICO"

El doctor Jorge Toro, jefe del Departamento de Epidemiología del Ministerio de Salud estuvo en Antofagasta, junto a dos expertos norteamericanos del Hospital Walter Reed que trabajan buscando una vacuna. En esa oportunidad, señaló a reporteros de este diario que se trataba de un "brote epidémico", lo que ratificó en los últimos días en la capital.

También señaló que las autoridades estaban encarándo este problema con la mayor seriedad y que en Antofagasta se estaban concentrando esfuerzos. Colocó como ejemplo la misma presencia del proyecto Walter Reed, para buscar una vacuna, un programa para la detección de portadores y el trabajo de vigilancia y prevención que desarrolla el Servicio de Salud.

El año 1987 en Antofagasta se produjeron 8 casos de meningitis meningocócica, el 88 la cifra subió a 13 y el 89, se llegó a los 29. La alerta roja estaba encendida. En 1991 se registraron 47 casos y la incidencia por 100 mil habitantes llegó a 12,1, la más alta hasta el momento.

¿Cómo puede definirse una enfermedad que en cuatro años sube de 8 a 47 pacientes?



En tanto, para la Direc-

## SE TRATA DE EVITAR LA EPIDEMIA

● Existe un terror a la palabra epidemia. Salud dice que no se han presentado casos secundarios. A principio de año murieron dos niños que jugaban juntos en el lapso de 13 días. Exámenes de portadores entregará un panorama más preciso. Hace dos semanas que no hay casos en la capital regional

ción del Servicio de Salud de Antofagasta, el desafío es tomar las medidas adecuadas para evitar "los ribetes trágicos de una epidemia declarada".

Optimistas en la visión del problema, destacan que "no tenemos ni hemos tenido casos secundarios y en ningún establecimiento educacional se ha presentado más de un caso simultáneo". Los médicos definen como "secundarios" los casos en que el germen se transmite de una persona a otra. Esta es una condición para que se pueda hablar de epidemia.



## ¿Y LA VACUNA?

Para el doctor Antonio Cárdenas Tadiach, jefe del equipo médico que trabaja en el laboratorio montado para buscar una vacuna antimeningitis, el problema es "obtener un producto que proporcione una inmunidad notablemente superior a los conseguidos hasta ahora, que no superan el 54 por ciento".

"Nuestro trabajo no se limita a los resultados con la vacuna que desarrollamos, sino que estamos informados de los avances más recientes que se están dando en el mundo, por parte de otros equipos que trabajan con el mismo fin".

A nivel nacional, una comisión encabezada por el doctor Luis Martínez, jefe del Departamento de Programas del Ministerio de Salud, partió con destino a La Habana, para conocer el terreno los avances experimentados por la vacuna cubana, que ha tenido muchos simpatizantes en nuestro país.

## ¿FATAL COINCIDENCIA?

Si bien Salud afirma que

no hay casos secundarios, en la población Libertad existió gran inquietud a principios de año, por el deceso de dos menores en un lapso de trece días.

Ellos se conocían, tenían contacto y vivían a no más de dos cuadras de distancia. Esta situación generó alarma y a nivel de vecinos se planteó el problema a las autoridades de Salud.

Todavía no estaba implementado, (aún no lo está totalmente), un plan para detección de portadores. Habría sido útil saber si existían otros menores del sector que tenían el meningococo en su organismo. De todas formas, el procedimiento profiláctico llevado a cabo por el Servicio fue efectivo y no se volvió a presentar el problema.

Por último, la novedad con respecto a los programas que desarrollan las autoridades de Salud es precisamente este programa para la detección de portadores, el que va a permitir conocer cuan generalizado está el meningococo tipo B en segmentos de la población que podrían estar más expuestos.

El doctor Antonio Cárdenas Tadiach, jefe del programa Wair en Antofagasta para obtener una vacuna antimeningitis, trabaja. Mientras tanto, una comisión del Ministerio de Salud viaja a Cuba para ver como van los progresos allá.



Entre la vida y la muerte pequeña de población Bonilla

# Una lactante está muy grave por meningitis

Página

## Una niña de siete meses se encuentra entre la vida y la muerte en el hospital por meningitis

Una niña de siete meses se encuentra entre la vida y la muerte en el Hospital Regional. Esta afectada por meningococcemia, una enfermedad meningocócica de alta letalidad, en la que el germen ataca todo el organismo.

En la sala de recuperación de pediatría, en el sexto piso del Hospital Regional, se encuentra internada desde la noche del lunes una menor residente en el sector de la Bonilla.

De acuerdo a los antecedentes que se pudieron recoger, la niña fue trasladada al Servicio de Urgencia del centro asistencial afectada por los temidos síntomas. En ese lugar se le diagnosticó el mal, quedando internada.

Una vez realizados los exámenes se pudo comprobar que la niña se encontraba afectada por meningococcemia, una enfermedad de alta mortalidad, en la que el meningococo ataca la totalidad del organismo.

Inmediatamente en el centro asistencial se tomaron las medidas con el objeto de salvar la vida de la menor, mientras que a nivel del Servicio de Salud se dio curso al tratamiento profiláctico a sus contactos, el cual ya fue realizado.

Consultado el doctor Antonio Cárdenas Tadiach, jefe del Proyecto Wrair para obtener una vacuna contra la meningitis, el profesional confirmó este nuevo caso, señalando:

"Efectivamente, se encuentra internada una menor de siete meses afectada por meningitis meningocócica. Su estado es grave y ya han sido tomadas las medidas que la situación amerita".

También dijo que se trata del caso número 17 que se presenta durante este año en la ciudad de Antofagasta.

### CASO NUMERO 26

Con respecto a la situación regional, de acuerdo a las estadísticas que ha dado a conocer el Servicio de Salud de Antofagasta, se trataría del caso número 26 durante el presente año.

Cabe señalar que a igual fecha el año pasado los afectados ascendían a 36, por lo cual aún se mantiene una notoria disminución con respecto al año 1992.

De las 26 personas que han contraído la enfermedad en este año, seis han fallecido, dos menores de la población Libertad, un adulto del sector Estación, una menor de la avenida Mejillones, un funcionario público y un menor del sector sur.

De estas seis personas, cinco han dejado de existir debido a meningococcemia, mientras que otras dos se han salvado. Es decir, de siete meningococcias, cinco pacientes han fallecido y dos han sido mantenidas con vida.



El doctor Antonio Cárdenas Tadiach, jefe del laboratorio WRAIR que busca una vacuna antimeningitis, confirmó un nuevo caso del temido mal en Antofagasta.

**Deceso se registró en el Hospital de Antofagasta**

# Nueva víctima fatal por el brote de meningitis

Falleció, a pesar de los esfuerzos médicos, la lactante que permanecía desde el martes internada en el Hospital Regional, a raíz de un cuadro respiratorio, que luego derivó en una meningococcemia, informó el doctor Alex Arroyo Meneses, Director subrogante del Servicio de Salud de Antofagasta, quien lamentó el desenlace fatal e insistió en los resguar-

dos que debe tomar la población para evitar el contagio.

Señaló el facultativo que con el caso letal, aumentan a 7 las personas fallecidas por meningitis meningocócica, todas en la capital regional. Antofagasta lidera la tasa de la II Región con 16 casos y en la región los afectados por el mal suman 28, durante el presente año.

**Página 5**

*EL MERCURIO, Jueves 19 de agosto de 1993*

## Murió lactante afectada por una meningococcemia

Pese a los esfuerzos médicos por salvar la vida a la lactante de 7 meses, que fue internada el martes en el Hospital Regional, a raíz de un cuadro respiratorio, que luego derivó en una meningococcemia, falleció a pocas horas de comenzado el tratamiento.

La información emanó del doctor Alex Arroyo Meneses, Director subrogante del Servicio de Salud de Antofagasta, quien lamentó el desenlace fatal e insistió en los resguardos que debe to-

mar la población para evitar el contagio.

Señaló el facultativo que con el caso letal, aumentan a 7 las personas fallecidas por meningitis meningocócica, todas en la capital regional. Antofagasta lidera la tasa de la II Región con 16 casos y en la región los afectados por el mal suman 28, durante el presente año.

Reiteró que no hay casos notificados como sospechosos o confirmados en el resto de las localidades de la región de Antofagasta.

Insistió sobre las pre-

cauciones en el sentido de evitar los contagios, no exponiendo a los menores en lugares donde se producen aglomeraciones, hacinamiento y poca ventilación.

Por su parte el doctor Antonio Cárdenas, encargado del laboratorio de Vigilancia de la Meningitis, confirmó que los contactos de la menor recibieron el tratamiento quimioprofiláctico, con el nuevo esquema impuesto por el Servicio de Salud, el cual es más moderno y más rápido en su aplicación.

Doctor Cárdenas anunció nueva etapa en estrategia para enfrentar el problema

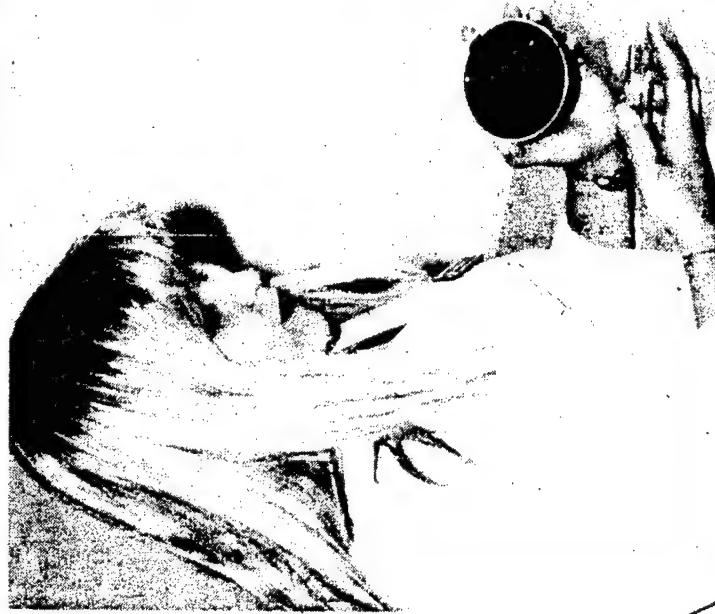
# Inician búsqueda de portadores de meningitis

● 200 antofagastinos serán examinados, comenzando por personal hospitalario. Posteriormente se efectuará en los grupos que sean considerados como de mayor riesgo.

Desde el primero de septiembre, pacientes, estudiantes y pobladores.

La iniciativa está inserta dentro de la estrategia de acción contra la meningitis que en portadores sanos. La muestra abarcará a 200 personas, entre las que se incluirá personal hospitala-

bilidad en Antofagasta y el



La enfermera del laboratorio WRAIR muestra los receptáculos especiales, donde se desarrollará el cultivo bacteriano.

Servicio de Salud de esta capital regional.

Detalles de este nuevo programa fueron entregados por el doctor Antonio Cárdenas Tadih, jefe del laboratorio WRAIR en Antofagasta, quien ha estado coordinando este proceso con la autoridades de Salud.

"El primero de septiembre, el hospital Walter Reed junto al Servicio de Salud de Antofagasta agregará una nueva estrategia para combatir la meningitis meningocócica en Antofagasta. Con este fin se va a iniciar un estudio de portadores sanos del meningococo tipo B en poblaciones de más altos riesgos.

"Se comenzará con los servicios de urgencia, recuperación de pediatría y la UCI del hospital, para después determinar en que poblaciones se continuará. Podría tratarse de un colegio, un sector, ...de acuerdo a los casos que se pudieran presentar.

"Con esto, se está asumiendo una nueva modalidad en el tratamiento del problema. Ya amplió el concepto de contacto, se cambió la quimio—profilaxis por una más sencilla y eficiente. En esta nueva etapa, vamos a salir a buscar el meningococo en portadores sanos", explicó el doctor Cárdenas.

Consultado con respecto al cambio realizado en la quimio—profilaxis, el especialista señaló que en reemplazo de la rifamicina, se había adoptado la cefixima, que se usa en una sola dosis, no como lo que sucedía con la anterior. "Su uso ha sido coordinado con el Instituto de Salud Pública en Santiago", detalló.

## TAMBIEN PARTICULARES

También se le preguntó si el examen de portadores sanos podría ser solicitado por personas en forma particu-



La toma de la muestra es bastante sencilla. Los primeros en realizarla será personal de organismos de Salud. En forma privada, a lo tras tomar un examen de frotis. En lo fundamental que respondió: "Se puede haber, pero habría que coordinar con los laboratorios privados, con el fin de ponerse de acuerdo en una técnica simple e indoloro, la que posteriormente es analizada, tras un desarrollo de cultivos bacterianos.

Este análisis se realiza

# Dramática batalla de menor con meningitis

EL MERCURIO, Martes 31 de agosto de 1993

## Teresita se aferra a la vida en dura lucha contra meningitis

Con mucho optimismo los médicos tratantes del Servicio de Pediatría del Hospital Regional, recibieron el quinto día desde que una lactante de 5 meses de edad, está siendo tratada para liberarla de una meningococcemia, estado fulminante de la enfermedad por meningococos.

Según el último parte, la niña está evolucionando bien, dentro de su gravedad, lo que abre esperanzas de una posible recuperación. Sin embargo, según el doctor Antonio Cárdenas, encargado del laboratorio de vigilancia permanente de la enfermedad, la guagua está muy delicada y el diagnóstico es reservado.

La lactante ha sobrevivido durante cinco días al ataque fulminante de la enfermedad por cuanto llegó al centro asistencial de la capital regional con una meningococcemia, enfermedad

que dentro de las 48 horas iniciales, por lo general es letal.

Este es el caso 29 de meningitis que se produce en la II Región y representa el noveno por meningococcemia, de los cuales seis fueron letales y dos salvaron con vida, constituyéndose la guagua en el tercero, si es que su fortaleza le permite soportar los embates de la enfermedad.

Teresita, así es su nombre, ha logrado acaparar la atención y el cariño del equipo médico que la atiende, quienes se han consituído en un férreo aliado para tratar de salvarle la vida.

Los médicos están optimistas, pero su diagnóstico es reservado y no quieren aventurarse, aunque la niña ha tenido reacción favorable al tratamiento instaurado por los médicos tratantes del

Servicio de Pediatría del Hospital Regional.

Ellos señalaron que hay buenos signos vitales, por lo tanto tienen un optimismo reservado, ya que aún está muy grave, sin embargo las esperanzas de salvarla aún no se pierden.

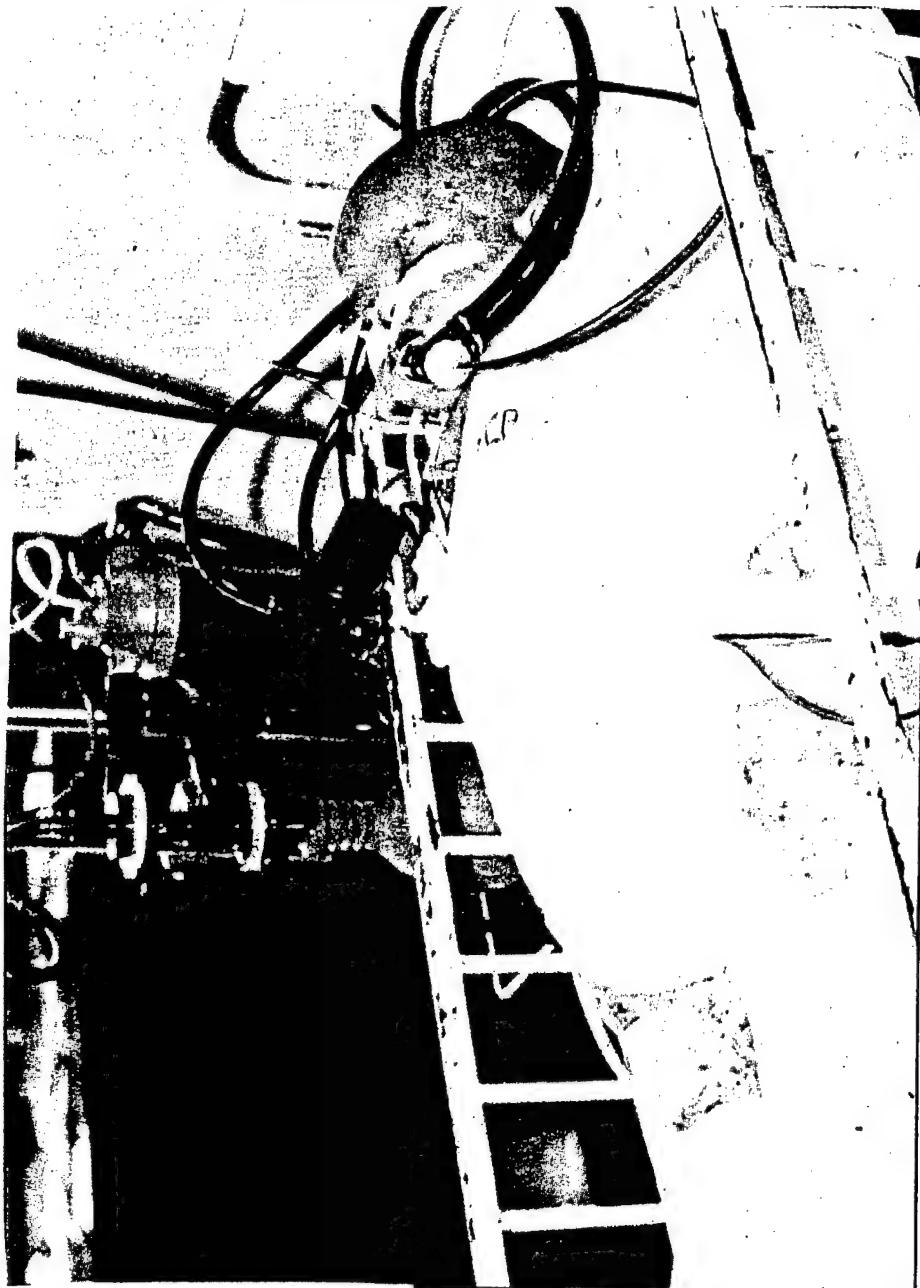
La oración de las voluntarias que acuden al Servicio y de muchas personas que han conocido el caso a través de este Diario, parece que están influyendo en la reacción de la menor. Así lo señaló una de las enfermeras que la atiende y que le ha entregado mucho cariño.

Mientras tanto, Teresita, sigue conectada a un ventilador mecánico y con un fuerte tratamiento a base de antibióticos, para cortar la infección.

De esta forma se debate entre la vida y la muerte, pese a sus pocos meses de vida.

no estado de salud

03/09/93



Antofagasta, Viernes 3 de septiembre de 1993

Una impresionante lucha por la vida está dando Teresita, la menor de cinco meses afectada por una meningococcemia que permanece desde hace una semana internada grave en la UCI del Hospital Regional.

**Nueva víctima del flagelo. Cifra de pacientes se elevó a treinta**

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# **Meningitis atacó a otra menor de edad**

La Estrella del Norte 03/04/83

## Graves siguen las dos niñas con meningitis

En grave estado permanecen las dos menores afectadas por meningococcemia en el Hospital Regional de Antofagasta. La menor tocopillana de cinco años que está hace una semana muestra algunos síntomas de mejoría, mientras que la niña antofagastina de 3 años 8 meses se encuentra en etapa crítica.

Ambas están en la UCI pediátrica, donde los médicos desarrollan un impresionante esfuerzo por sacarlas adelante, a pesar de la letalidad que presenta la afección.

De acuerdo a antecedentes que se pudieron obtener, diez han sido los pacientes que en el presente año han sufrido meningococcemia en la región de Antofagasta. De ellos seis han fallecido, dos se recuperaron satisfactoriamente y las últimas dos son las que permanecen internadas en estado grave.

Estos 8 pacientes son parte de los 30 que hasta el momento han contraído la enfermedad ocasionada por el meningococo tipo B en la región y que la colocan en la de más alta incidencia en estos momentos en el país.

El hecho que las dos niñas se encuentren con vida constituye una verdadera hazaña médica, debido a que la meningococcemia alcanza rangos de 90 por ciento de letalidad.

Se dijo que el éxito que se ha logrado hasta el momento se debe a la capacidad lograda por los médicos antofagastinos, quienes ya llevan años tratando este tipo de problemas. El Servicio de Salud ha desplegado todo un procedimiento que permite abordar con la mayor rapidez hasta la sospecha por meningitis.

**Doctor Antonio Cárdenas analizó la medida tomada en la capital del país**

## Rechazo a la vacuna cubana coincide con política de salud antofagastina

La decisión ministerial de no utilizar la vacuna cubana contra la meningitis, coincide con la posición que han mantenido las autoridades de salud de Antofagasta con respecto a este tema. Así lo dio a conocer el doctor Antonio Cárdenas Tadich, jefe del proyecto WRAIR en Antofagasta, que busca una vacuna contra el mal.

El especialista fue consultado ante la decisión de no utilizar una vacuna cubana o de otra nacionalidad, en forma de masiva entre los chilenos, para atacar el brote epidémico que afecta al país.

Cárdenas Tadich se manifestó bastante satisfecho por la resolución, debido a que

corresponde a la posición que ha sostenido tanto el equipo que trabaja a sus órdenes, como el Servicio de Salud de Antofagasta.

—Doctor, ¿qué le parece la decisión ministerial de no usar la vacuna cubana?

—Coincide con lo que hemos sostenido. No reúne las condiciones que se necesitan para ser aplicadas a la población y controlar un brote de meningitis tipo B. Avala lo que sostienen las autoridades locales de salud y viene a ratificar el estudio muy profundo y detallado que se hizo, el cual es de acuerdo con lo que se sabe en la comunidad médica internacional.

—Si de hecho no se va a utilizar la vacuna cubana, ¿qué se va a hacer a cambio?

—A nivel de Antofagasta, epidemiológicamente se sabe que los brotes duran como promedio diez años. Aquí ya se ha recorrido la mitad de este camino, por lo que nos hallamos en mejores condiciones en comparación a otras zonas como la central, que recién está viviendo este problema. Se debe continuar insistiendo y mejorando todas las medidas estratégicas que las autoridades de salud local han implementado para controlar este brote.

—¿Por qué ustedes sostienen que la vacuna cubana

no era conveniente?

—Fuera del fundamento científico que se ha logrado recopilar durante todo este tiempo, existe el antecedente que dicha vacuna fue aplicada en Brasil. Allí no dio resultados y fue abandonada. También hay que considerar que la inversión de 80 millones requerida era muy grande en relación a los resultados que nos podría brindar.

De esta forma, el doctor Cárdenas entregó su impresión acerca de la medida tomada en Santiago, que no dio luz verde a una vacunación masiva con suero cubano a la población chilena.

Nicole tenía 3 años y falleció ayer en el Hospital Regional

# Murió menor con meningitis

Página 5

## Murió menor afectada por meningitis

Ayer a mediodía dejó de existir en el Hospital Regional, Nicole, una de las dos menores que estaban internadas en ese centro asistencial, afectadas por una meningococcemia.

El deceso se produjo a las 13 horas, pese al esfuerzo del equipo médico que le estaba suministrando el tratamiento.

Con el fallecimiento de la pequeña, de 3 años 8 meses de edad, la cifra de muertos en la Región,

aumenta a 8 casos en lo que va corrido del año, lo que demanda una mortalidad del 42 por ciento en Antofagasta, donde los casos suman 19. En la región la cifra se eleva a 30 casos.

Por otra parte, la pequeña Teresita, de tan sólo 5 meses de vida, sigue debatiéndose entre la vida y la muerte. Sin embargo en las últimas horas, experimentó una leve mejoría dentro de su gravedad y fue retirada del respirador me-

cánico y ahora respira por sus propios medios.

La niña fallecida vivía en la calle Tarapacá, ubicada en el sector norte de la capital regional y fue internada en grave estado la semana pasada, aquejada por una meningococcemia aguda.

Mientras tanto, Teresita, con igual diagnóstico, que llegó de Tocopilla, ha tenido una evolución favorable dentro del estado crítico en que se encuentra.

# Lactante de cinco meses aún lucha contra la meningitis

Un error médico derivado de la no detección a tiempo de la enfermedad, habría provocado la muerte de la menor, Nicole Tapia Rojas, afectada por una meningococcemia. La acusación la formuló su madre Paola Ro-

jas Martínez, quien señaló que en la Posta del Hospital Regional no supieron reconocer la meningitis y en los primeros momentos el diagnóstico fue de alergia.

Con el sufrimiento que demanda la pérdida de su

única hija, Nicole, de 3 años y 8 meses de edad, la joven mujer contó su drama y denunció la presunta negligencia que habría llevado a la niña a la muerte.

En su hogar de calle Tarapacá 4558 ubicado en la

población Norte de Antofagasta y mientras en el living es velada la pequeña en un ataúd blanco, rodeado de flores llevadas por amigos, parientes y vecinos, la atribulada madre, con un incipiente embarazo de tres meses, aceptó relatar su drama a periodistas de "El Mercurio".

Y entre sollozos, recordó el fatídico lunes 30 de septiembre cuando llevó a su pequeña a la Asistencia Pública.

Eran las 6 y media de la mañana y esperó más de una hora a que la atendieran. La niña se había enfermado la noche antes y presentaba un cuadro febril, fuertes dolores de cabeza y manchas rojizas en todo el cuerpo.

Luego del primer diagnóstico señalado como alergia, la menor quedó hospitalizada. Sin embargo, dijo, fue demasiado tarde cuando se dieron cuenta que tenía meningitis y estaba grave. "Porque mi pequeña ya estaba en coma cuando me dijeron que padecía de meningococcemia. Entonces hablé con la enfermera y le dije que se habían equivocado. Me respondió que conversara con el médico y si no estaba conforme que retirara a Nicole".

Agregó, "estoy segura que el médico confundió las manchas de una alergia, con las de la meningitis, de lo contrario mi hija no estaría hoy en ese ataúd. Fue demasiado tarde cuando se dieron cuenta y la sometieron a tratamiento".

Nicole, vivía en casa de su abuela, con su madre y su padre, Claudio Tapia Vásquez, estudiante. Era la reglona de todos los parientes y vecinos del sector.

La angustiada madre, hizo un llamado a la comunidad y dijo "ahora ya nada se puede hacer por mi hija, pero lo único que pido es que los médicos reconozcan la enfermedad a tiempo, para que otros padres no sufran lo que yo estoy sufriendo ahora y puedan salvar a sus hijos a tiempo".

El funeral de la pequeña víctima del flagelo que afecta a Chile, se efectuará hoy a las 10 de la mañana.

EL MERCURIO, Martes 7 de septiembre de 1993

## Seremi justificó decisión del Ministerio sobre vacuna cubana

El Secretario Regional Ministerial de Salud, doctor Mario Besnier Hernández, fue enfático al señalar que la decisión de no aplicar masivamente la vacuna cubana, no es política, ni de recursos. Obedece exclusivamente a problema técnico.

Aseguró que el Ministerio de Salud, tiene reservas económicas suficientes para campañas masivas y que en la resolución se tomó en cuenta la experiencia de Iquique y Antofagasta.

Agregó que las comisiones médicas que viajaron a Cuba, Brasil y Finlandia, fueron determinantes para la decisión ministerial, por

cuanto hicieron las evaluaciones en el terreno, donde se aplicaron vacunas contra el meningococo tipo B, que es el que afecta a Chile.

Los facultativos trajeron conclusiones y ello motivó resolver la no aplicación masiva en nuestro país.

Con los antecedentes se formó una comisión técnica nacional, que analizó los informes de los grupos viajeros.

Comentó "lo manifestado por el señor Ministro corresponde a lo que ya suponíamos que se dictaminaría, por cuanto no es el mo-

mento adecuado de aplicar una vacuna masiva. Esto, porque si bien en Chile hay incremento del número de casos, hay tasas más elevadas que las anteriores, el problema de la meningitis meningocócica no reviste un carácter epidémico explosivo y el comportamiento habitual es que en los próximos meses los casos debieran disminuir. Además la comisión tomó muy en cuenta los resultados de Iquique y fundamentalmente de Antofagasta, donde los Servicios de Salud, han sido capaces de controlar la enfermedad, evitando que se transforme en epidemia".

**¡AQUI ESTA EL MENINGOCOCO! En los frasquitos que están siendo manipulados se encuentran las muestras de cultivos con las bacterias halladas en laboratorio. Tres portadores sanos en cien muestras tomadas ha sido el resultado de un minucioso trabajo de investigación científica realizado en el Laboratorio de Meningitis del WRAIR, diseñado para pesquisar cuán extendido está el meningococo B.**



**¡Otro caso de meningitis en la ciudad!**

# **NIÑITO GRAVE**

**Total subió a 24**

# Confirmaron los dos casos de meningitis

Página 8

## Salud confirmó los 2 casos de meningitis

El Servicio de Salud, confirmó los dos casos de meningitis detectados entre el jueves y el viernes de la semana pasada en Antofagasta.

El primero es una meningitis bacteriana de germen desconocido y el otro corresponde al tipo meningocócica, con lo que la cifra en la capital regional se ve aumentada en 24 casos, en lo que va corrido del año. Esta cantidad es inferior a la del año pasado a la misma fecha, en que se registraron 33.

La información fue entregada por el doctor Antonio Cárdenas Tadich, quien resaltó que la población no debe bajar la guardia

respecto a tomar las medidas preventivas contra la enfermedad.

Esta afectó a una menor de un año 5 meses de edad, la que el pasado jueves fue internada en la Unidad Pediátrica de Cuidados Intensivos, siendo sometida a tratamiento, al cual respondió bien y ahora se encuentra fuera de peligro, comprobándose que se trata de una meningitis bacteriana, pero de germen desconocido.

Un día después llegó hasta el establecimiento su prima de 5 años. Sin embargo ambas viven distante, pero por el lazo familiar se temió en un principio de que se tratase de un caso secundario, lo que quedó descartado.

La niña fue sometida a tratamiento, se le comprobó meningitis meningocócica y ahora se recupera en forma satisfactoria.

El médico reiteró el llamado a la comunidad en el sentido de evitar los contagios manteniendo las habitaciones ventiladas e iluminadas con luz natural. A la vez que ocupar vasos y otros utensilios para dar bebida a los niños, cuando ya han sido usados. También se debe evitar toser frente a los menores y si se hace se debe tapar la boca.

De esta forma, señaló el facultativo, hay menos opción a que los menores reciban el germen que pueda desarrollarse en las meninges.

**Nuevo caso conmueve a la región en menos de 24 horas**

# Menor de pocos meses grave por meningitis

EL MERCURIO, Miércoles 5 de enero de 1994

Página 9

## Otro caso de meningitis conmueve a la II Región

Un nuevo caso de meningitis detectado en un menor de 6 meses de edad, conmueve al sector Salud, ante el rebrote inesperado de la enfermedad en la II Región.

Este paciente fue internado el domingo pasado en la Unidad de Cuidados Intensivos de Pediatría del Hospital Regional y pertenece a la capital regional, habiéndose ubicado su domicilio en el sector norte de la ciudad.

A el se agrega el de la lactante de 25 días proveniente de Tocopilla, la cual, según informes médicos, se encuentra en grave estado y estable dentro de esta situación de salud.

El nuevo caso es una meningitis bacteriana la que aún no ha sido determinada su etiología, lo que significa el origen de la enfermedad, lo cual podría quedar decidido hoy, según el resultado de los exámenes practicados al

lactante.

Por su parte la menor de 25 días aún sigue conectada a respirador artificial y está convulsionada, de acuerdo a lo informado por fuentes de Salud.

Por otra parte se espera que en las próximas horas se pueda determinar la etiología de su enfermedad, ya que fueron pedidos hemocultivos a Tocopilla, lugar desde donde proviene la bebé.

Comunicado 21/02/99

**Primer caso fatal del presente año se registró en Antofagasta**

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# **Menor falleció por meningitis**

En grave estado se encuentra un menor de 13 años, proveniente de la población Bonilla, afectado por una meningococcemia, enfermedad meningocócica que junto a la meningitis, produce preocupación en Antofagasta.



## Grave en la UCI menor de 13 años con aguda meningitis

26/3/94

Ayer en la mañana fue internado en la UCI del Hospital Regional de Antofagasta un menor de 13 años, afectado de meningococcemia. Aún no se establece el tipo de germen que provocó la enfermedad, pero el niño se encuentra en condiciones graves.

De acuerdo a lo señalado por el jefe de Pediatría de ese establecimiento, doctor Antonio Cárdenas Tadich, también director del laboratorio WRAIR, el menor fue llevado a la posta de urgencia, donde se le diagnosticó en forma inmediata el mal.

El menor proviene de una de las ampliaciones del sector Bonilla y unas quince horas antes de presentarse en el recinto, comenzó a manifestar síntomas. Estos consistieron en alta fiebre, náuseas y decaimiento generalizado.

"Se trata de una meningococcemia de tipo fulminante. El paciente llegó con shock séptico en estado caliente, con compromiso de su estado general y lesiones en la piel de tipo purpúricas", manifestó el especialista.

El cuadro hizo necesario que quedara aislado en la UCI, donde se le están entregando todas las atenciones necesarias, a fin que supere su gravísimo estado.

El doctor Cárdenas señaló que de confirmarse mediante los exámenes de laboratorio que se trata de una enfermedad provocada por el meningococo tipo B, sería el sexto caso que se presenta en Antofagasta.

La meningococcemia al igual que la meningitis, puede ser provocada por el meningococo tipo B y otros agentes. La diferencia entre ambas es que la meningitis consiste en la inflamación de las meninges, mientras que meningococcemia es un ataque generalizado al organismo.

Es por eso que esta última enfermedad es gravísima, ya que suele tener tasas de mortalidad que se acercan al 100 por ciento. Una de sus características es la aparición de pequeñas manchas en la piel cuando empieza a manifestarse. Tiene desarrollos fulminantes, que a veces no superan las doce horas.

LA ESTRELLA DEL NORTE

# Estudio de portadores sanos de meningitis reveló rango normal

**A**l culminar la primera etapa del estudio realizado a portadores sanos del meningococo que produce la meningitis meningocócica, éste reveló que existe una tasa con cifras dentro de los rangos normales, pero que está discretamente elevada.

La información emanó del doctor Antonio Cárdenas Tadich, presidente del Comité Regional de Vigilancia de la Meningitis y encargado del laboratorio que estudia los antecedentes para una vacuna.

El médico señaló que el proyecto se realizó en la escuela D-65 y fue un trabajo destinado a conocer la tasa de niños que pudieran ser portadores de la bacteria que produce la meningitis.

Agregó que el colegio fue elegido "porque había antecedentes de casos ocurridos en el plantel educacional y por otra parte está inserto en el sector norte que es el área donde se ha focalizado los mayores casos de la enfermedad. Asimismo, de esta forma se da una respuesta técnica a la inquietud existente en esa comunidad escolar".

Destacó que para abor-

dar la problemática el Comité conjuntamente con el Servicio de Salud, diseñó un estudio para conocer la realidad del problema y determinar la existencia de algún foco, o simplemente desecharlo de plano.

La realización del programa duró 40 días, se tomó muestras a 210 niños de un universo de mil 300. De los muestreados 18 resultaron ser portadores de la bacteria, a los cuales se les aplicó el tratamiento y a la semana, mejoraron. Ello reveló una tasa de 8,3 por ciento. "Cifra que está dentro de rangos normales, discretamente elevada".

De esta forma, dijo el médico, se descarta definitivamente a la escuela como foco de infección. Sin embargo, se mantiene el seguimiento a los portadores por 9 meses, para conocer el comportamiento epidemiológico.

Destacó que si se hubiese logrado una cifra mayor, se habría tomado medidas, porque el problema no es de toda la comuna, sino de un sector que tiene altos índices.

Asimismo señaló que de acuerdo al cuadro comparativo, la enfermedad registró en Antofagasta, 17 casos en 1992; 13, en 1993 y a la fecha 7, de los cuales uno con resultado de muerte, en lo que

va corrido del presente año.

Explicó que durante el estudio se tomó diariamente a 5 niños por cursos y en dos de ellos, se estableció que de los 5 hubo 3 que fueron portadores de la bacteria. "Ante esta situación hicimos el tratamiento quimioproláctico al curso completo".

Respecto a la vacuna que está en estudio en el Instituto Walter Reed de Estados Unidos, indicó que en diciembre próximo podrá haber una respuesta sobre una nueva dosis, por cuanto la anterior no dio los resultados esperados.

Finalmente el médico dijo, que aunque la enfermedad mantiene su curva descendente, la población no debe descuidarse y observar las recomendaciones para prevenirla, por los brotes epidémicos de una enfermedad, que por lo general tienen una duración de 10 años. "Por lo tanto como técnicamente el brote comenzó en 1987, ya llevaríamos 7 años. Asumimos que la población ha generado defensas e inmunidades y por lo tanto el problema tendría que aminsonar".

EL MERCURIO

MARTES 5 DE JULIO DE 1994

El Mercurio de Antofagasta  
día : 08-12-92.

## En marzo probarán en la ciudad vacuna contra meningitis tipo B

En marzo del próximo año será aplicada y probada en Antofagasta una nueva vacuna contra la meningitis tipo B.

El anuncio lo hizo el doctor Jorge Toro Albornoz, jefe del Departamento de Epidemiología del Ministerio de Salud, quien llegó a la ciudad acompañado por los médicos Robert Alan Kushner y Wendel Zollinger, del Hospital Walter Reed de Washington, Estados Unidos, pioneros en la búsqueda de antidotos para este mal y quienes están trabajando en el proyecto inmunológico para esta variante de la enfermedad.

Precisó el doctor Toro que la administración de la dosis se hará a 200 niños en edad escolar de entre a 12 a 15 años, previa autorización de sus padres por cuanto serán voluntarios y corresponderá a la primera etapa cuya administración ya se efectuó en Estados Unidos a un centenar de menores, que no experimentaron rechazo ni complicaciones. Sin embargo en Norteamérica, no tienen la enfermedad y por tal motivo se hace necesario aplicar la vacuna en menores

que viven en una zona donde anualmente se presenta, como promedio, cerca de medio centenar de casos.

Por su parte los facultativos norteamericanos explicaron que el Instituto Walter Reed inició ahora la segunda etapa del estudio, la que consiste en verificar la respuesta inmunológica de quienes recibieron la dosis.

Asimismo, el doctor Toro, aclaró que la fase que se aplicará en Antofagasta es la primera etapa ya realizada en el país del norte y que su aplicación "por ningún motivo tiene carácter de experimento".

Para verificar el grado de efectividad de la nueva vacuna, se implementa actualmente un laboratorio en el Hospital Regional, destinado a pesquisar la reacción de los voluntarios y acumular el seguimiento de muestras, bajo la vigilancia epidemiológica y experiencia obtenida por investigadores mundiales.

El centro de obtención de datos, está a cargo del doctor Antonio Cárdenas Tadih, quien coordina el proyecto en Antofagasta.

Los médicos, Wendel Zollinger, Jorge Toro Albornoz, María Cristina Rojas y Robert Alan Kushner, dieron a conocer los alcances de la nueva vacuna contra la meningitis.



Todos los enfermos son menores de ocho años

# OTROS 3 CASOS DE MENINGITIS

● Detectados durante primeros días del año; no hay explosión infecciosa.

Tres nuevos casos simultáneos de meningitis fueron detectados en la Región, durante los primeros días de este año. Uno de ellos es de Mejillones y los otros dos corresponden a Antofagasta.

La doctora María Cristina Rojas, jefa del Departamento Programa de las Personas del Servicio de Salud, aseguró que la aparición de estos nuevos enfermos, todos

menores de 8 años, no significa una explosión infecciosa, por cuanto no se relacionan entre sí.

Expresó que los casos corresponden a meningitis meningocócica tipo B y que a los menores que contrajeron el mal se les aplicó el tratamiento adecuado y se recuperan en forma satisfactoria.

Página 5

26, - 70 - 90

República de Chile  
Servicio Salud Alta  
M. Miranda  
Hoyeño w/RAIR.

El Director de Salud descartó en forma categórica que haya epidemia

# MENINGITIS: VAN 44 CASOS EN LA REGIÓN

● Tasa es inferior a 1991: Iquique, Antofagasta y Aysén están a la cabeza.

El doctor Manuel Zamorano Godoy, Director del Servicio de Salud de Antofagasta, descartó en forma categórica que la II Región esté frente a una epidemia de meningitis meningocócica. Dijo que pese a tener este año 44 casos, la tasa es de 11.1 inferior a la del año pasado que fue de 12.1. Y si se hace una proyección de acuerdo a cómo se está

dando la enfermedad, probablemente la tasa llegue alrededor de 15 por cien mil habitantes. Reconoció que aunque el guarismo es

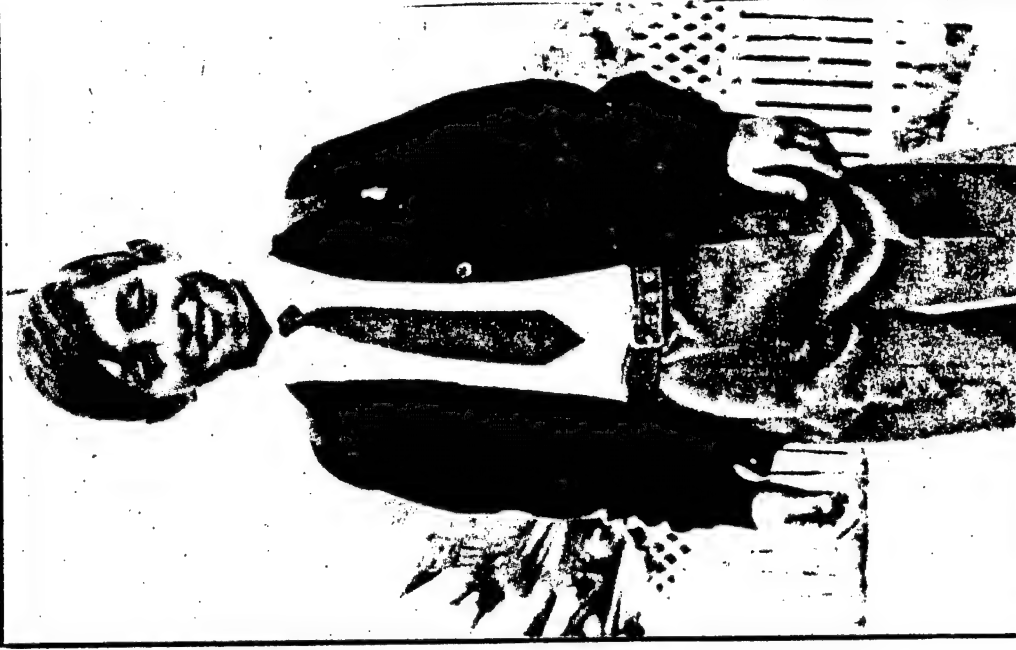
alto a nivel del país en general, en ningún caso está al tope de las estadísticas por cuanto es Iquique quien sigue manteniendo la peor situación. **Página 5**

Memorio  
Antofagasta  
9-11-92

**Escolar antofagastino de 11 años perdió la vida en solamente 24 horas después de ser atacado por el virus**

# **FULMINANTE MUERTE POR MENINGITIS**

Vea Pág. 8



Una desesperada odisea protagonizan los padres del escolar antofagastino que murió víctima de un ataque fulminante de meningitis. La fotografía muestra a Juanito Rojas Fritis cuando la vida le sonreía plenamente y nadie pensaba que alguna vez podría ser protagonista de una historia trágica.

## Nuevo caso fatal en Antofagasta

# MENINGITIS MATO A MENOR

Vea Pág. 7

*Crónica/7*

**También se anunció un nuevo caso en el Hospital**

## Menor de un año dejó de existir debido a un cuadro de meningitis

Una menor de un año afectada por meningitis falleció ayer en Antofagasta. La información fue entregada por fuentes de salud, quienes aclararon que el germen que produjo el deceso es un estreptococo, no contagioso, y que no se trata de la meningitis meningocócica que causa preocupación en la Región.

También se señaló que una menor de 8 años se encuentra afectada por la enfermedad, pero que hasta el momento, no se sabe la naturaleza del germen que la ocasionó.

La información fue proporcionada por el Médico Jefe del Proyecto Vacuna contra la Meningitis, doctor Antonio Cárdenas Tadic. La entidad mantiene actualizada todos los casos que se van produciendo en la región.

Ante la consulta realizada, el doctor Cárdenas confirmó el fallecimiento de una menor de 1 año, debido a un cuadro de meningitis. La niña ingresó el 2 de junio, dejando de existir el 5 de este mes.

"Debo dejar claro que esta meningitis fue producida por un estreptococo y no por el meningococo B. Este germen ocupa el segundo lugar en letalidad por meningitis en el país, pero en el caso específico de Antofagasta, el meningococo B es el que concentra la atención", señaló el especialista.

Explicó el doctor Cárdenas que ante la enfermedad desarrollada por este germen, no es necesario realizar el procedimiento de profilaxis a la familia, tan necesario en el caso de las enfermedades meningocócicas. Tampoco este deceso es considerado en las estadísticas que se llevan a este objeto.

El doctor Cárdenas también confirmó la hospitalización de una niña de 8 años, que ingresó a pediatría del Hospital Regional. El diagnóstico clínico señala un cuadro de meningitis y actualmente se encuentra en tratamiento y aislada. Se esperan los resultados de los exámenes, los que debieran señalar cual fue el germen que la produjo.

# MÉDICOS PREPARADOS PARA LUCHA FRONTAL CONTRA LA MENINGITIS

EL MERCURIO, Domingo 13 de junio de 1993

CARLOS HERRERA ASTORGA

El brote de meningitis detectado en Antofagasta, si bien es cierto, no está catalogado como una epidemia, desde el año 1987 a la fecha ha experimentado un notorio aumento de casos registrados en la II Región. Por este motivo el Servicio de Salud de Antofagasta, inició en colaboración con el Instituto Walter Reed de Estados Unidos, un programa destinado a elaborar una vacuna que sirva de antídoto para combatir la enfermedad, que a la fecha ostenta cinco casos fatales en Antofagasta.

Antiguamente su sola aparición provocaba pánico en la población y hoy aún viven personas que por haberla contraído mantienen secuelas, aunque con el tiempo han ido desapareciendo, todavía son notorias en ellas.

Pero la ciencia médica ha avanzado considerablemente en la búsqueda de medicamentos que mitiguen el sufrimiento, salven a la persona y no dejen secuelas en ella, aún persisten los casos fatales y contra ellos nada se ha descubierto. Porque, lamentablemente, su acción es fulminante y en pocas horas se pierde una vida.

Conscientes de lo que significa la enfermedad, sobre todo en la población menor, el equipo multidisciplinario que abordó la tarea de recopilar muestras, procesar antecedentes y traspasarlos al organismo norteamericano que en definitiva procesará el antídoto, ha logrado a la fecha considerables adelantos. Sin embargo, la vacuna aún no está lista y hay un retraso aproximado de un par de meses, por cuanto se estima que en agosto podría producirse en forma masiva, pero ahora por problemas técnicos, se espera que su producción no sea posible hasta fin de año.

Para conocer aspectos del trabajo que realizan los profesionales de la salud en torno a estos estudios, recurrimos al doctor Antonio Cárdenas Tadiach, 38 años de edad, a cargo del Laboratorio de Vigilancia Epidemiológica de la Meningitis, quien además es pediatra y magister (c) en Salud Pública con mención en epidemiología, titulado en la Escuela de Medicina de la Universidad de Chile.

¿Con qué objetivo se implementó el

laboratorio?

"Desde el año 1987, hemos observado un aumento progresivo de los casos de meningitis provocada por el meningococo, en la II Región y especialmente en Antofagasta. En ese año hubo 8 casos y el pasado terminó con 47. Esa es la razón por la que iniciamos esta vigilancia.

Este es un problema de salud pública, que afecta a una comunidad y se expone a un riesgo mayor de sufrir la enfermedad.

Para tener claro el problema debemos señalar que la meningitis meningocócica está catalogada en trece tipos que son provocados por meningococos, de ellos cinco los que producen enfermedades en el hombre. Aparte de eso se caracterizan por ser epidémicos.

Por lo tanto se instalan en una comunidad y tienden a aumentar los casos, lo que nos está pasando a nosotros.

Los que producen la enfermedad son el A, B, C, Y y W-135. para combatirlos el año 1979 el Instituto Walter Reed de Estados Unidos, confeccionó una vacuna contra el cero grupo A y el C. El año 1982, generaron una vacuna tetravalente contra los grupos A, C, Y y W-135; pero contra el único grupo que no existe vacuna, en el mundo, es el B.

Ese es el germen que nos está dando problemas en Antofagasta, Iquique y otras zonas del país con menor intensidad. En Iquique el año 1987 probaron una vacuna y tuvo una eficacia de 51 por ciento, lo que significa que no fue muy buena.

El meningococo tipo B, es responsable del 90 por ciento de las causas de meningitis por meningococo. Lo mismo sucede en Estados Unidos que tiene el problema, pero de ninguna manera en la magnitud que lo poseemos nosotros. De allí su interés en encontrar una vacuna. También se ha detectado casos en Noruega, Finlandia, Brasil y Cuba, que lo tuvo en 1987.

Como éste es un problema epidemiológico de salud pública, se combate en primer lugar, como no hay vacuna, con medidas que se toman para controlar un caso, el que además de tratarlo, se trata a las personas que viven cerca, llamados contactos del enfermo, para evitar que les de meningitis. Y

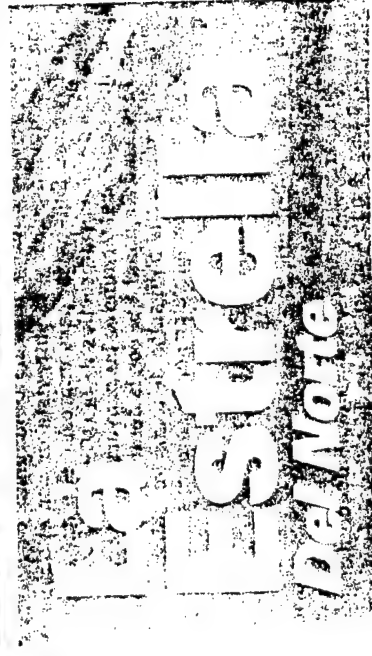


Un moderno laboratorio tiene el Servicio de Salud, para extraer y mantener las muestras que sirven para elaborar una vacuna contra la meningitis.



Así era en vida Guillermo Mardalaga Navia, funcionario de Serviu que falleció inesperadamente de una meningitis, causando conmoción en diversos círculos antofagastinos.

**Apreciado antofagastino falleció víctima del mal. Hondo pesar en el Serviu; Club Hípico y amplios sectores de la comunidad.**



# **MENINGITIS MATO A UN FUNCIONARIO**

*El Mercurio de Antofagasta  
Miércoles 23/06/93*

**Pequeños pacientes ingresaron al Hospital de Antofagasta**

# **2 NUEVOS CASOS DE MENINGITIS**

Viernes 25 de junio de 1993

La entula del Norte.

**Niña de cinco años se recupera satisfactoriamente**

## **Meningitis aún no es confirmada por los exámenes de laboratorio**

Hasta ayer por la tarde, todavía no existía confirmación de laboratorio con respecto a la menor sospechosa de tener meningitis meningocócica, que podría convertirse en el caso número 21 del presente año. La información fue entregada por el doctor Antonio Cárdenas Tadich, jefe del proyecto "Vacuna contra la Meningitis".

Señaló el médico que se trata una menor y no un varoncito, como se había dicho inicialmente. Ella tiene 5 años, es mejillonina y su caso fue detectado en Calama. Desde el hospital Carlos Cisternas fue derivado al Regional de Antofagasta, donde actualmente se encuentra recuperándose.

Explicó el doctor Cárdenas que el examen clínico efectuado indica que se trata de meningitis meningocócica, por las características que presenta, pero que se requiere de la

confirmación de laboratorio y los resultados que se han obtenido no han ratificado hasta el momento dicho diagnóstico.

No obstante, señaló que la menor se ha recuperado notablemente, lo que constituye una tranquilidad para el equipo que la está tratando.

Consultado por una tocopillana que fue trasladada hasta Antofagasta afectada por meningitis, el especialista confirmó la situación, pero aclaró que ésta fue producida "por estreptococos", por lo cual no puede ser incluida entre el mal que preocupa a los antofagastinos, generados por el meningococo B.

También el médico informó que aparte de estos casos, de acuerdo al chequeo que realizan en todos los establecimientos asistenciales diariamente, no se han presentado nuevos casos sospechosos de meningitis.



**Mediante un registro computarizado el jefe del programa "Vacuna contra la Meningitis", doctor Antonio Cárdenas Tadich, controla el desarrollo de este mal.**

**EL MERCURIO, Domingo 27 de junio de 1993**

**Dueña de casa de 29 años falleció en Antofagasta**

# **MENINGITIS: 6 CASOS FATALES**

**Página 5**

Jueves 8 de julio de 1993

*La Estrella del Norte*

**¡Confirman el mal en dos mujeres antofagastinas!**

# GRAVES POR MEVINGTIS

Jueves 8 de Julio de 1993

**Antofagastinas contrajeron el mal que preocupa a la comunidad**

# **MENINGITIS: HAY DOS NUEVOS CASOS**

Página 5

Lunes 12 de julio de 1993

La estrella de Noche.

Ayer en Antofagasta. Contador, también afectado por mismo mal, está grave

# GUAGUA MURIO VICTIMA DE MENINGITIS

Página 10

Guagua de tres meses falleció en el Hospital.  
Contador se halla grave en Cuidados Intensivos.

## MENINGITIS:

Una guagua de tres meses que fue llevada al Servicio de Urgencia del Hospital Regional, falleció a las pocas horas de ingresada, a consecuencia de una fulminante meningitis. Se dijo que se trataba de una meningococcemia ocasionada por el meningococo tipo B.

De acuerdo a las informaciones que se pudieron obtener, desde la calle Matías Rojas hasta el principal centro asistencial fue conducido el lactante F.G., debido a lo que parecía un fuerte resfío, que le había generado un cuadro febril.

Tras el examen realizado, el especialista de turno inmediatamente diagnosticó la enfermedad meningocócica, por lo que se le brindaron las atenciones respectivas, siendo aislado y tomadas las muestras de rigor.

No obstante, el mal se encontraba avanzado, por lo cual la vida del pequeño no se prolongó más allá de las dos de la tarde, tras ser internado.

El deceso del lactante se produjo alrededor de las 14 horas, a pesar de los esfuerzos realizados para salvarle la vida.

De ser confirmada hoy como meningococo B el germen que produjo la muerte del menor antofagastino, se trataría de la

sexta muerte en lo que va corrido del año.

Por tratarse de una meningococcemia, se trataría de la quinta muerte por esta causa, entre las seis registradas.

Hasta el momento, han fallecido dos menores de la población Libertad, un adulto del Sector Estación, una menor de la población Oriente y un conocido funcionario de la población Bonilla. Los tres menores y el residente de la población Bonilla dejaron de existir por meningococcemia, un ataque generalizado en el organismo por parte del meningococo B. Igual suerte habría corrido la guagua recientemente fallecida.

### OTRO CASO GRAVE

Un contador de 60 años se encuentra internado en la Unidad de Cuidados Intensivos del Hospital Regional de Antofagasta, debido a un cuadro de meningitis que lo mantiene en grave estado. Se debería al meningococo tipo B, aún cuando no se ha podido obtener la versión del Servicio de Salud.

De acuerdo a los antecedentes que se pudieron obtener, el antofagastino se hallaba resfriado desde un lapso superior a

una semana. El sábado comenzó a sentirse bastante mal, por lo que fue llevado hasta el Servicio de Urgencia del Hospital Regional, donde se le brindó la atención respectiva.

En el lugar, se le diagnosticó clínicamente un cuadro de meningitis, por lo que de inmediato fue internado en la UCI, donde ayer por la tarde se hallaba en estado estacionario.

Aún cuando no fue posible conseguir información el centro asistencial, se supo que se le habían efectuado los exámenes, con el objeto de identificar el tipo de meningitis que lo afectaba, pero que las características apuntan con cierta seguridad hacia el meningococo tipo B.

Se estima que durante la mañana de hoy, el Servicio de Salud entregará información al respecto, confirmando tanto el fallecimiento del lactante como este caso, el número 24 de ser meningocócica, o descartándola, si se trata de un agente diferente.

De tratarse ambas de enfermedades meningocócicas, las estadísticas consignarían para este año un total de 25 casos, de los cuales seis pacientes habrían fallecido.

Jueves 15 de julio de 1993

# Meningitis: no hay avances en vacuna

## ● Especialistas visitaron Antofagasta

Un atraso en el desarrollo de la vacuna contra la meningitis, por respuestas inferiores a las esperadas en el proceso experimental efectuado en Estados Unidos y un plan de estudios de portadores que se implementará en Antofagasta, fueron los dos más importantes anuncios efectuados por el Jefe del Departamento de Epidemiología del Ministerio de Salud, doctor Jorge Toro, en la visita que efectuó ayer a la región.

El doctor Toro viajó acompañado de dos especialistas del hospital estadounidense "Walter Reed", los doctores Kischner y Zollinger, los doctores Kischner y Zollinger. Esta entidad desarrolla en conjunto con el Ministerio de Salud, una vacuna contra la meningitis para Antofagasta.

La comisión fue recibida en Antofagasta por el doctor Antonio Cárdenas Tadich, médico a cargo del programa en Antofagasta. Sostuvieron una reunión que se prolongó por varias horas, en el Laboratorio Wrair, su centro de investigaciones en la capital regional.

Pasado el mediodía, el representante del Ministerio junto a los especialistas extranjeros, conversaron con este diario, para dar a



A la izquierda, los especialistas norteamericanos Kischner y Zollinger, a su lado el Jefe de Epidemiología del Ministerio de Salud, doctor Jorge Toro. Al extremo derecho, el jefe del proyecto en Iquique y a su lado, el anfitrión, doctor Antonio Cárdenas, junto a su equipo de trabajo.

conocer el estado en que se encuentra el proyecto.

"El trabajo que se está desarrollando con el hospital "Walter Reed" en el desarrollo de una vacuna que proteja efectivamente a la población es muy serio. Hay necesariamente etapas, la primera es un trabajo con animales, la segunda es con voluntarios en Norteamérica, la tercera es mucho más fina y considera la calidad

de respuestas del sistema inmunológico con voluntarios en Antofagasta e Iquique", explicó el doctor Toro.

"La primera etapa de desarrollo de esta vacuna había andado bien en animales, sin embargo, la segunda no ha resultado del todo satisfactoria, con una protección de alrededor de un cincuenta por ciento, lo cual se considera que no es adecuado, por lo tanto se está ajustando otra

línea de investigación, buscando precisamente cuál sería la vacuna que proteja más de un cincuenta por ciento. Eso es lo que se está buscando, por lo tanto va a haber una tardanza, una postergación en conseguir una vacuna".

Otro de los aspectos que abordó el representante del Ministerio fue un plan de estudios de portadores, que se está estudiando implementar en Antofagasta.